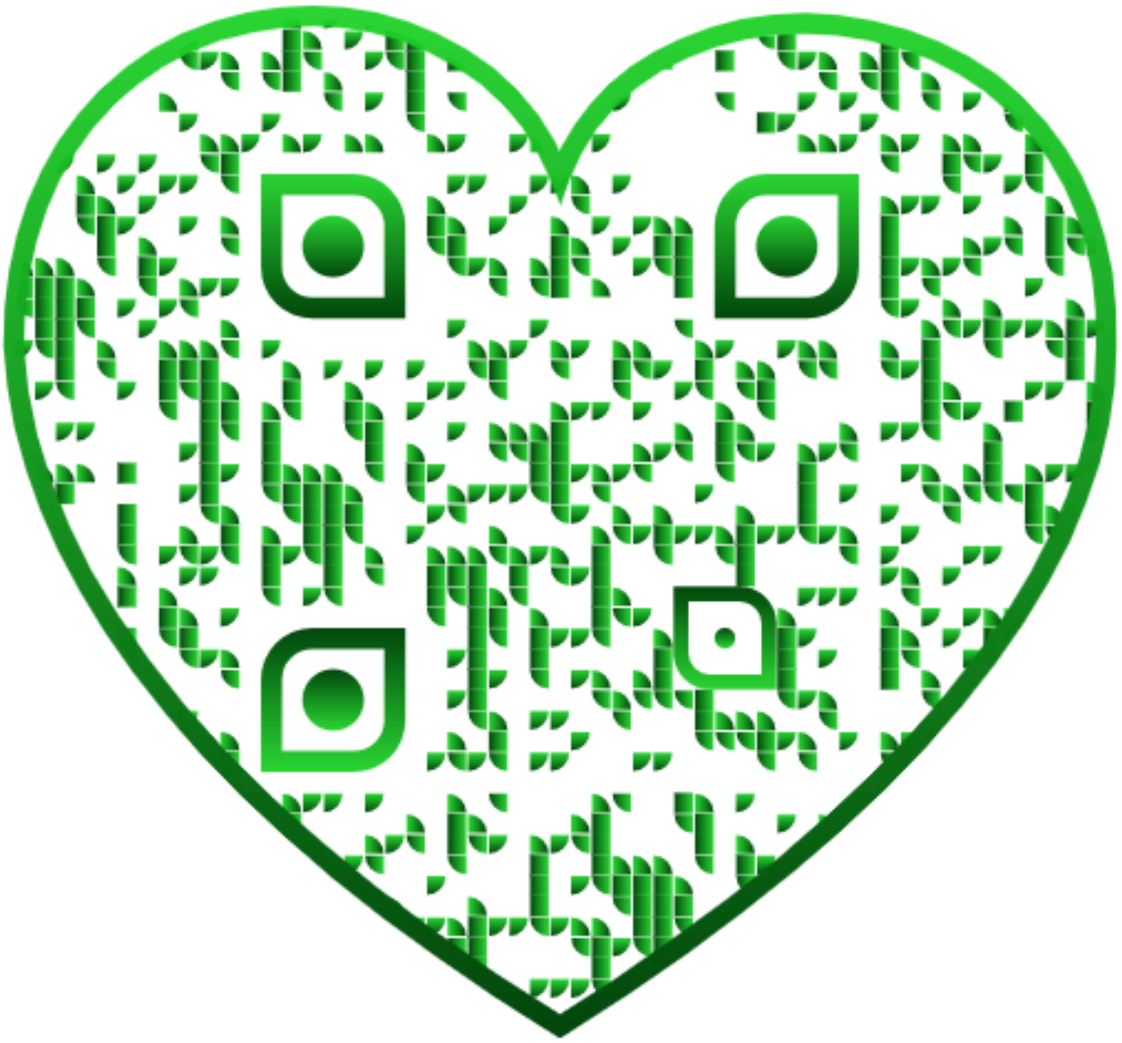


Pharmacotherapy Flash Cards

238 Q&A cards sharpen your therapeutic decision-making skills

Jeremy L. Johnson • Michelle E. Condren
Kimberly M. Orosby • Ann E. Lloyd • Kelly Murray

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Preface

The purpose of the *Pharmacotherapy Flash Cards* is to aid pharmacy and other health professional students in the practice of pharmacotherapeutic decision making using case studies. As faculty members of the University of Oklahoma, College of Pharmacy, we use case studies all throughout our curriculum to allow students to apply newly learned information. Case studies can bring an element of real-life clinical practice into the classroom and help students to start thinking like clinicians. Repeated exposure to this way of thinking can only help to develop and polish critical-thinking skills that will be used throughout students' careers. We want to bring this element to students so they can test their pharmacotherapeutic knowledge and hone their skills anytime they want.

Pharmacotherapy Flash Cards provides a comprehensive review of pharmacotherapeutic concepts for each of the major disease states commonly encountered by clinicians in practice. Essentially, it condenses the highlights and clinical pearls from therapeutics courses or modules in pharmacy schools to emphasize appropriate, evidence-based therapeutic decision making and drug therapy monitoring. A standard formatted case on the front of each card introduces students to a systematic flow of thinking when gathering patient health information and builds toward making therapeutic recommendations or decisions. Cases are designed to put the future healthcare provider into different potential scenarios where therapeutic decisions must be made (eg, a pharmacy, clinic, provider office visit, hospital, etc.).

Each case is followed by a therapeutic question. The answer may call for a specific drug or a general drug class. Many aspects of the case must be considered to determine the most appropriate answer. This may include past medical history, medication history, allergies, physical exam and other studies, and laboratory or other test results. To accommodate different learning styles, some questions are asked directly,

while others are presented in a multiple-choice format. At the top of the back of each card is the answer to the question—either a drug or drug class with each agent in the class listed. This is followed by drug information commonly used or considered when using these medications. This includes the mechanism of action, contraindications, precautions, adverse effects, and monitoring parameters. The back of each card also includes a section called "Case Notes" where the answer to the case is explained along with other clinical pearls about use of the drug or drug class, management of the disease, and dosing.

We want to bring a quality and meaningful learning tool that students will find to be valuable and convenient to use. These flash cards may be used as an adjunct to information learned in the classroom while students review for exams, or even as a review tool when preparing for the licensure examination. Aside from using these cards to solve clinical cases, some students may find value in simply studying the backs of cards for general recognition of routine drug information.

We are proud to present *Pharmacotherapy Flash Cards* as a current and evidence-based learning tool. We are confident students will find this to be a valuable tool for reviewing drug information and for developing critical-thinking skills and an approach to clinical decision making. We believe these flash cards will help many students through challenging therapeutics courses while enhancing retention of knowledge through application in real clinical scenarios. We are excited to receive feedback from our readers and welcome comments on how to improve upon this study tool in the next edition.

Acknowledgments

We would like to thank the editors at McGraw-Hill for their expertise and assistance in bringing this publication to fruition.

We would like to thank the faculty and administrative staff of the University of Oklahoma College of Pharmacy for their support and guidance throughout this process. We especially appreciate Dr. Shane Desselle for identifying this opportunity and for his encouragement and enthusiasm throughout the project.

Finally, we would like to thank our family and friends for their understanding and support throughout this experience.

About the Authors

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Dr. Kimberly Crosby has served as a faculty member for the University of Oklahoma College of Pharmacy, Department of Clinical and Administrative Sciences since July 2002. Prior to coming to OU, she held the position of Assistant Professor for Southwestern Oklahoma State University College of Pharmacy from 2000 to 2002. Dr. Crosby received her Bachelor of Sciences in Pharmacy from Southwestern Oklahoma State University in 1990

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Dr. Ann Lloyd is an Assistant Professor at the University of Oklahoma College of Pharmacy, Department of Clinical and Administrative Sciences in Tulsa. She received her Doctor of Pharmacy degree in 2003 from the University of Kansas and completed a pharmacy practice residency at Barnes-Jewish Hospital/Washington University Medical Center in St. Louis. She is a Board-Certified Pharmacotherapy Specialist. Dr. Lloyd currently serves as the clinical pharmacy specialist in Infectious Diseases at Saint Francis Hospital in Tulsa. Her area of practice focuses on antimicrobial stewardship. In addition to her clinical service, Dr. Lloyd teaches in the College of Pharmacy Therapeutics courses. Her primary areas of interest and research are antimicrobial stewardship, pharmacodynamics, and teaching critical thinking and problem solving.

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Abbreviations

5-HT	serotonin
AACE	American Association of Clinical Endocrinologists
ABG	arterial blood gases
ACE	angiotensin-converting enzyme
ACIP	Advisory Committee on Immunization Practices
ADA	American Diabetes Association
ADHD	attention deficit hyperactivity disorder
AED	antiepileptic drugs
AIDS	acquired immunodeficiency syndrome
AlkPhos	alkaline phosphatase
ALT	alanine aminotransferase
AML	acute myelogenous leukemia
AMP	adenosine monophosphate
ANC	absolute neutrophil count
APAP	acetaminophen
ARB	angiotensin receptor blocker
ASA	aspirin
AST	aspartate aminotransferase
ATP-III	Third Adult Treatment Panel
AV	atrioventricular
BB	beta-blocker
BCG	bacille Calmette-Guérin vaccine
BNP	brain natriuretic peptide
BP	blood pressure
BPH	benign prostatic hyperplasia
BSA	body surface area
BUN	blood urea nitrogen
Ca	calcium
CABG	coronary artery bypass graft
CAD	coronary artery disease
CBC	complete blood count
CCB	calcium channel blocker
CCR5	specific HIV cellular binding site
CD	Crohn's disease
CF	cystic fibrosis
CHC	combined hormonal contraceptive

CHF	chronic heart failure
CHOP	cyclophosphamide, hydroxydaunorubicin (doxorubicin), Oncovin (vincristine), and prednisone/prednisolone
Cl	chloride
Clcr	creatinine clearance
CNS	central nervous system
CO_2	carbon dioxide
COMT	catechol-O-methyl transferase
COPD	chronic obstructive pulmonary disease
COX	cyclooxygenase
CP	chest pain
CPK	creatine phosphokinase
CPT	chest percussion therapy
CR	controlled release
CRP	C-reactive protein
CT scan	computed tomography scan
CTA	clear to auscultation
CVD	cerebrovascular disease
CVP	central venous pressure
CXCR4	specific HIV cellular binding site
CYP	cytochrome P450
DHP	dihydropyridine
DKA	diabetic ketoacidosis
dL	deciliter
DMARD	disease-modifying antirheumatic drug
DNA	deoxyribonucleic acid
DPP-IV	dipeptidyl peptidase IV
DVT	deep vein thrombosis
DXA	dual-energy x-ray absorptiometry
ECG	electrocardiography
ED	erectile dysfunction
EE	ethinyl estradiol
EEG	electroencephalogram
ELISA	enzyme-linked immunoabsorbent assay
ESR	erythrocyte sedimentation rate
ESRD	end-stage renal disease
F	Fahrenheit

FDA	Food and Drug Administration
FEV1	forced expiratory volume in 1 second
FSH	follicle-stimulating hormone
FT_4	free thyroxine
FVC	forced vital capacity
G6PD	glucose-6-phosphate dehydrogenase
GABA	gamma-aminobutyric acid
GERD	gastroesophageal reflux disease
GI	gastrointestinal
GLP-1	glucagon-like peptide 1
Glu	glucose
GYN	gynecologist
H pylori	*Helicobacter pylori*
HA	headache
HAV	hepatitis A virus
HBV	hepatitis B virus
Hct	hematocrit
HDL	high-density lipoprotein
HFA	hydrofluoroalkane
Hgb	hemoglobin
HIPA	heparin-induced platelet aggregation
HIV	human immunodeficiency virus
HLA	human leukocyte antigen
HMG-CoA	3-hydroxy-3-methylglutaryl-coenzyme A
HPA	hypothalamic-pituitary-adrenal
HPV	human papillomavirus
HR	heart rate
Ht	height
HTN	hypertension
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
IBW	ideal body weight
IgA	immunoglobulin A
IgE	immunoglobulin E
IL-2	interleukin 2
IM	intramuscular
In	inches
INR	international normalized ratio
IPV	inactivated polio vaccine
IV	intravenous
JNC-7	Seventh Joint National Committee

K	potassium
KPhos	potassium phosphate
LABA	long-acting beta$_2$ agonist
LAIV	live attenuated intranasal vaccine
Lbs	pounds
LDL	low-density lipoprotein
LFT	liver function tests
LH	luteinizing hormone
LHRH	luteinizing hormone-releasing hormone
MAO	monoamine oxidase
MAP	mean arterial pressure
mcg	microgram
MCV	mean corpuscular volume
MDI	metered-dose inhaler
mEq	milliequivalent
Mg	magnesium
mg	milligram
MI	myocardial infarction
mL	milliliter
mmHg	millimeters of mercury
MMR	measles mumps rubella
MRSA	methicillin-resistant *S. aureus*
MS	multiple sclerosis
Na	sodium
NCEP	National Cholesterol Education Program
NE	norepinephrine
NH_3	ammonia
NH_4	ammonium
NIH	National Institutes of Health
NKDA	no known drug allergies
NNRTI	nonnucleoside reverse transcriptase inhibitor
NPH	neutral protamine hagedorn
NRT	nicotine replacement therapy
NRTI	nucleoside reverse transcriptase inhibitor
NSAID	nonsteroidal anti-inflammatory drug
NSCLC	non-small cell lung cancer
NSTEMI	non-ST-segment elevation myocardial infarction

NTG	nitroglycerin
NYHA	New York Heart Association
O_2 sat	oxygen saturation
OA	osteoarthritis
OB	obstetrician
OCD	obsessive compulsive disorder
OTC	over the counter
PAOP	pulmonary artery occlusion pressure
PCP	primary care provider
PDE	phosphodiesterase
PE	pulmonary embolism
PEF	peak expiratory flow
PEG-ELS	polyethylene glycol electrolyte lavage solution
PI	protease inhibitor
PIP	proximal interphalangeal
Plt	platelet
PN	parenteral nutrition
po	by mouth
PO_4	phosphate
ppd	pack per day
PPI	proton pump inhibitor
PPSV	pneumococcal polysaccharide vaccine 23-valent
PR	ECG deflection
PRN	as needed
PSA	prostate-specific antigen
PT	physical therapy
PT	prothrombin time
PTH	parathyroid hormone
PTT	partial thromboplastin time
PUD	peptic ulcer disease
PUVA	psoralen and ultraviolet light
PVD	peripheral vascular disease
QRS	ECG deflection
QTc	corrected QT interval
RA	rheumatoid arthritis
RAAS	renin-angiotensin-aldosterone system
RBC	red blood cell
REM	rapid eye movement
RNA	ribonucleic acid
RR	respiratory rate

RSV	respiratory syncytial virus
SABA	short-acting beta$_2$ agonist
SCr	serum creatinine
SERM	selective estrogen receptor modulator
SG	serum globulin
SIADH	syndrome of inappropriate antidiuretic hormone
SLE	systemic lupus erythematosus
SOB	shortness of breath
SQ	subcutaneous
SSRI	selective serotonin reuptake inhibitor
STEMI	ST-segment elevation myocardial infarction
SVR	systemic vascular resistance
T	temperature
T_4	thyroxine
Tbili	total bilirubin
TC	total cholesterol
TCA	tricyclic antidepressant
Td	diphtheria and tetanus toxoids
Tdap	tetanus, diphtheria, and acellular pertussis vaccine
TG	triglyceride
TIA	transient ischemic attack
TIV	trivalent inactivated influenza vaccine
TMJ	temporomandibular joint
TMP-SMZ	trimethoprim-sulfamethoxazole
TNF	tumor necrosis factor
TPMT	thiopurine methyltransferase
TPN	total parenteral nutrition
TSH	thyroid-stimulating hormone
TT_4	total thyroxine
TZD	thiazolidinedione
U-100	100 units/1 mL
U-500	500 units/1 mL
UC	ulcerative colitis
UVB	type B ultraviolet
VIP	vasoactive intestinal peptide
VL	viral load

VRE	vancomycin-resistant enterococcus
VTE	venous thromboembolism
VQ	ventilation/perfusion
VZV	varicella zoster virus
WBC	white blood cell
WHO	World Health Organization
WNL	within normal limits
Wt	weight
XR	extended release

Adult Reference Values for Laboratory and Other Tests

SERUM PLASMA

A1c, hemoglobin	4.0-5.6%
Albumin	3.2-5 g/dL
AlkPhos	33-131 IU/L
ALT	10-35 IU/L
Ammonia	20-70 mcg/dL
Amylase	30-110 units/L
AST	20-48 IU/L
Bilirubin, direct	0-0.3 mg/dL
Bilirubin, total	0.1-1.2 mg/dL
BUN	7-20 mg/dL
Calcium	8.6-10.3 mg/dL
Chloride (Cl)	95-108 mEq/L
Cholesterol, total	<200 mg/dL
CO_2	23-30 mEq/L
CPK	8-150 IU/L
Creatinine (Cr)	0.5-1.4 mg/dL
CRP	<0.8 mg/dL
Ferritin	13-300 ng/mL
Folate	3.6-20.0 ng/dL
Glucose, fasting	70-100 mg/dL
HBV DNA	undetectable
HDL cholesterol	>40 mg/dL
IgE	<114 kU/L
Iron	65-150 mcg/dL
Iron binding capacity	250-420 mcg/dL
Lactic acid	0.7-2.1 mEq/L
LDL cholesterol	<70, <100, <130, <160 mg/dL
Lipase	23-208 units/L
Magnesium (Mg)	1.6-2.5 mg/dL
Osmolality	289-308 mOsm/kg
Phosphate	2.8-4.2 mg/dL
Potassium (K)	3.5-5.2 mEq/L
Protein, total	6.5-7.9 g/dL
Sodium (Na)	134-149 mEq/L
Transferrin	>200 mg/dL
Triglycerides (TG)	45-150 mg/dL
Uric acid, female	2.0-7.5 mg/dL
Uric acid, male	2.0-8.0 mg/dL

CEREBROSPINAL FLUID

Glucose	50-70 mg/dL
Protein	15-45 mg/dL

URINE

Amylase	32-641 units/L
Creatinine	1,000-2,000 mg/24 h
Clcr, female	75-115 mL/min
Clcr, male	85-125 mL/min
Glucose	1 g/24 h
Iron	0.15 mg/24 h
Magnesium	146-209 mg/24 h
Microalbumin/Cr	<30 mcg/mg or mg/g
Osmolality	500-800 mOsm/kg
Oxalate	10-40 mg/24 h
Phosphate	400-1,300 mg/24 h
Potassium	25-120 mEq/24 h
Sodium	40-220 mEq/24 h
Protein	0.05-0.1 g/24 h

ARTERIAL BLOOD GASES (ABG)

pH	7.35-7.45
pCO_2	35-45 mm Hg
pO_2	70-100 mm Hg
HCO_3	19-25 mEq/L
TCO_2	19-29 mEq/L
O_2 sat	95-100%

COMPLETE BLOOD COUNT (CBC)

Hbg, female	12.0-15.0 g/dL
Hbg, male	13.5-16.5 g/dL
Hct, female	36-44%
Hct, male	41-50%
RBC, female	4.0-4.9 mill/mm^3
RBC, male	4.5-5.5 mill/mm^3
RDW	<14.5
MCV	80-100 fL
MCH	26-34 pg
MCHC	31-37%
Platelets	150-450 $\times$ 10^3/mm^3

WHITE BLOOD COUNT AND DIFFERENTIAL

White blood cell	4.5-11.0 × 10^3/mm^3
Segs	35-66
Bands	5-11
Lymphs	24-44
Monos	3-6
Eosinophils	0-3
Basophils	0-1
Atypical lymphs	0-8
NRBC	0

ERYTHROCYTE SEDIMENTATION RATE (ESR)

ESR, Westergren, female	0-20 mm/h
ESR, Westergren, male	0-15 mm/h
ESR, Wintrobe, female	0-15 mm/h
ESR, Wintrobe, male	0-10 mm/h

VITAL SIGNS

Blood Pressure (BP)	mm Hg
Adult	
normal	<120/<80
hypertensive	≥140/≥90
Pediatric	
normal	<90th percentile for age, height, and gender
hypertensive	>95th percentile for age, height, and gender
Heart Rate (HR)	beats per minute
Adult	60-100
Pediatric	
<1 week	91-166
1-3 weeks	107-182
1-2 months	121-179
3-5 months	106-186
6-11 months	109-169

1-2 years	89-151
3-4 years	73-137
5-7 years	65-133
8-11 years	62-130
12-15 years	60-119
Height (Ht)	inches (in)
Respiratory	breaths per minute
Rate (RR)	
Adult	12-18
Pediatric	
0-2 years	25-30
3-9 years	20-25
10-18 years	16-20
Temperature (T)	Fahrenheit (F)
	98.6
Weight (Wt)	pounds (lbs)

A 48-year-old man with a history of hypertension and Type 2 diabetes × three years comes to your clinic. He has been treating his hypertension with lisinopril/hydrochlorothiazide 20/25 mg po once daily. Over the last six months, his blood pressure control has worsened. At his last primary care provider (PCP) visit one month ago, his systolic blood pressure was elevated at 155/94 mmHg. Today, he presents to his visit for follow-up on his blood pressure. He has been compliant with diet, exercise, and medications.

Allergies: Nifedipine & nicardipine (rash, hives)

Medications: Multivitamin tablet (OTC) 1 po daily; lisinopril/hydrochlorothiazide 20/25 mg tablet 1 po daily; insulin NPH/regular 70/30 inject 50 units subcutaneously twice daily

Physical Exam/Other Studies:

Wt 197 lb Ht 74 in T 98.6°F BP 155/96 HR 72 RR 18 BMI 25.3
Physical exam is noncontributory. No evidence of target organ damage.
SCr 1.4 K 4.7 Clcr 65 MA 83
His PCP would like to begin an additional agent at this time.

Which of the following antihypertensive medications if added could raise his potassium?

A. amlodipine
B. atenolol
C. aliskiren
D. furosemide

Aliskiren	Renin inhibitor (no other agents in class)
Mechanism of Action	Inhibits renin, resulting in the blockade of the conversion of angiotensinogen to angiotensin I. This leads to decreased levels of angiotensin I and angiotensin II, which results in decreased aldosterone production and decreased vasoconstriction.
***Contraindications/* Precautions**	*Hypersensitivity, pregnancy category X*/History of angioedema, hyperkalemia, hypotension, severe renal impairment (GFR <30 mL/min, SCr >1.7 mg/dL – women and SCr >2 mg/dL – men), nephrotic syndrome, deteriorating renal function, or renal artery stenosis
Adverse Effects	Rash, hyperkalemia, diarrhea, creatinine kinase increases, BUN increases, cough
Drug Interactions	Cyclosporine, amifostine, rituximab, ketoconazole, MAO inhibitors, pentoxifylline, P-glycoprotein inhibitors/inducers, phosphodiesterase-5 inhibitors, diazoxide, prostacyclin analogs, furosemide, methylphenidate
Monitoring	Fluid status, blood pressure, serum electrolytes, BUN, creatinine
Case Notes	Aliskiren is a renin inhibitor that reduces blood pressure comparably to ACE inhibitors and ARBs. It is recommended as additional therapy for patients already on other first-line agents. Aliskiren can raise serum creatinine and potassium levels in patients, so these values should be monitored regularly. Caution should be used when combining aliskiren with other medications such as ACE inhibitors and ARBs, which may also raise potassium levels. Loop diuretics like furosemide will decrease serum potassium levels. Beta-blockers and calcium channel blockers like atenolol and amlodipine do not affect serum potassium levels. One benefit of aliskiren is that it is effective at reducing proteinuria and blood pressure in patients with diabetic nephropathy.

A 43-year-old man is returning to his physician for a follow-up visit to assess his blood pressure. At his last visit two weeks ago, his blood pressure was 150/95 mmHg, and he was instructed to exercise regularly and to try to control his diet as well. He was unaware that his blood pressure had been elevated until he saw his physician recently. He does not have any family history of hypertension, and he does not smoke. He drinks an occasional beer on the weekends. His medical history includes Type 2 diabetes and allergic rhinitis.

Allergies: NKDA

Medications: Phenylephrine 10 mg tablet (OTC) 1 po daily prn sinus congestion; metformin 1,000 mg tablet 1po twice daily

Physical Exam/Other Studies:

Wt 200 lb Ht 71 in T 98.6°F BP 152/96 HR 72 RR 18 BMI 27.9
Physical exam reveals no pertinent findings.
No abnormalities were seen on the ECG.
SCr 1.1 K 4.8 TC 230 LDL 163 HDL 35 TG 160 A1c 6.8
His clinic physician approaches you to help him choose the appropriate antihypertensive drug to start the patient on.

Which of the following antihypertensives would be most beneficial in this patient?

A. lisinopril
B. hydrochlorothiazide
C. amlodipine
D. diltiazem

Lisinopril	Angiotensin-converting enzyme inhibitors (benazepril, captopril, enalapril, fosinopril, moexipril, perindopril, quinapril, ramipril, trandolapril)
Mechanism of Action	Competitive inhibition of angiotensin-converting enzyme (ACE) that prevents the conversion of angiotensin I to angiotensin II. Reduction in angiotensin II levels results in a lowering of aldosterone production and decreased vasoconstriction.
***Contraindications/* Precautions**	*Hypersensitivity, history of angioedema, pregnancy category X*/Renal artery stenosis
Adverse Effects	Cough, hyperkalemia, dizziness, orthostasis, hypotension, angioedema, increased SCr
Monitoring	Blood pressure, BUN, serum creatinine, renal function, WBC, potassium levels. Additionally, if patient has renal impairment or collagen vascular disease, monitor CBC with differential.
Case Notes	ACE inhibitors are first-line agents used in the treatment of hypertension in diabetics. Other options, such as diuretics or calcium channel blockers may be as effective as ACE inhibitors but are not preferred over ACE inhibitors in diabetics. This is because ACE inhibitors provide renal protection in addition to decreases in blood pressure in diabetic patients. Agents and dosing in this class: lisinopril 10-80 mg daily; benazepril 10-40 mg daily; captopril 25-250 mg daily; enalapril 5-40 mg daily; fosinopril 10-40 mg daily; moexipril 7.5-30 mg daily; perindopril 4-16 mg daily; quinapril 10-80 mg daily; ramipril 2.5-10 mg daily; trandolapril 1-4 mg daily. Starting doses may be reduced by 50% for patients who are already on a diuretic or in the elderly. Risk of hyperkalemia is increased in patients taking other drugs, including but not limited to: potassium-sparing diuretics, angiotensin receptor blockers, or spironolactone. IV enalaprilat is used to treat hypertensive emergencies (dose: 1.25-5 mg every 6 hours). ACE inhibitors may cause a buildup of bradykinin, resulting in a dry cough that may be bothersome. If this occurs, angiotensin receptor blocking agents (ARBs) may be tried. ACE inhibitors may increase serum creatinine related to decreases in GFR. If the increase is 1 mg/dL or less in SCr no dosage or therapy changes are warranted.

A 43-year-old man returns to his physician for a follow-up visit to assess his blood pressure. At his last visit, he was started on lisinopril 10 mg po daily. He is complaining of a dry cough since beginning the lisinopril. At times, his cough is severe enough to disrupt his daily activities. His blood pressure is at goal today of <130/80 mmHg. His past medical history includes Type 2 diabetes and allergic rhinitis.

Allergies: NKDA

Medications: Loratadine 10 mg tablet (OTC) 1 po once daily prn sinus congestion; metformin 1,000 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 200 lb Ht 71 in T 98.6°F BP 125/80 HR 70 RR 16 BMI 27.9
Physical exam reveals no pertinent findings.
SCr 1.1 K 4.0 TC 230 LDL 163 HDL 35 TG 160 A1c 6.8

What class of agents could you switch to that would work similarly to ACE inhibitors and will not cause a cough?

Angiotensin Receptor Blockers (ARBs)	Candesartan, eprosartan, losartan, olmesartan, telmisartan, valsartan
Mechanism of Action	Blockade of the angiotensin II receptor resulting in a decrease in vasoconstriction and aldosterone release
***Contraindications*/ Precautions**	*Hypersensitivity to ARBs or a history of angioedema*/Pregnancy category X, renal artery stenosis
Adverse Effects	Hyperkalemia, hypersensitivity reactions, hypotension, angioedema, cholestatic jaundice, neutropenia/ agranulocytosis, renal function deterioration, hypertrophic cardiomyopathy, aortic stenosis, or unstable cardiovascular disease
Drug Interactions	Amifostine, lithium, rituximab, potassium salts, MAO inhibitors, NSAIDs, pentoxifylline, eplerenone, diazoxide, methylphenidate, prostacyclin analogs, tolvaptan, trimethoprim
Monitoring	Blood pressure, renal function, WBC, potassium; if patient has renal impairment or collagen vascular disease, monitor CBC with differential also.
Case Notes	Angiotensin receptor blockers and ACE inhibitors both exert their antihypertensive effects on the renin-angiotensin-aldosterone system (RAAS) by blocking aldosterone release and decreasing vasoconstriction. However, ARBs do not block the breakdown of bradykinin, which is responsible for the ACE inhibitor-induced cough. ARBs may be beneficial agents to try in patients who cannot tolerate cough but who are responding well to ACE inhibitor therapy. Dosing in this class: candesartan 8-32 mg/day; eprosartan 600-800 mg/day; irbesartan 150-300 mg/day; losartan 50-100 mg/day; olmesartan 20-40 mg/day; telmisartan 20-80 mg/day; valsartan 80-320 mg/day. Starting doses may be reduced by 50% for patients who are already on a diuretic or in the elderly. Risk of hyperkalemia is increased in patients taking other drugs, including but not limited to: potassium-sparing diuretics, ACE inhibitors, or spironolactone. Both ACE inhibitors and ARBs are beneficial to use in diabetics for their renal protective effects as well as their antihypertensive effects.

A 52-year-old African-American man presents for a follow-up on his hypertension. He has a history of seasonal allergic rhinitis, chronic constipation, and recently diagnosed hypertension. He has no other medical problems. He does not smoke cigarettes or drink alcohol. On physical examination during a visit three months ago with his primary care provider, blood pressures were 152/96 mmHg and 154/98 mmHg. After making diet and exercise improvements, he returned a month later to find his BP still elevated to 152/94 mmHg and 152/92 mmHg. He was diagnosed with hypertension and started on hydrochlorothiazide 12.5 mg daily. He returned a month later, and the hydrochlorothiazide was optimized to 25 mg daily because his BP was still not controlled to a goal of <140/90 mmHg.

He returns today for a follow-up visit on his hypertension. He reports adherence to his medication regimen and lifestyle modification plans.

Allergies: NKDA

Medications: Fluticasone 50 mcg spray once in each nostril twice daily; docusate 250 mg capsule (OTC) 1 po twice daily; hydrochlorothiazide 25 mg 1 tablet po every morning

Physical Exam/Other Studies:

Wt 225 lb Ht 70 in T 98.6°F BP 146/88 and 146/92 HR 88 RR 12 O_2 sat 98%

Physical exam reveals no pertinent findings.

Na 140 K 3.6 BUN 13 SCr 1.0 Glucose 88

The patient's BP has improved since the last medication adjustment, but is still not at goal. You decide additional drug therapy is necessary to continue to progress toward his goal BP.

What is the most appropriate drug class to add to his current regimen?

Dihydropyridine Calcium Channel Blocker (DHP CCB)	Amlodipine, felodipine, isradipine, nicardipine, nifedipine, nisoldipine
Mechanism of Action	Causes relaxation of vascular smooth muscle and coronary vasodilation by inhibiting calcium ions from entering the voltage-dependent calcium channels of vascular smooth muscle and myocardium during depolarization
***Contraindications*/Precautions**	*Hypersensitivity*/MI, angina, peripheral edema
Adverse Effects	Peripheral edema, flushing, headache
Drug Interactions	Substrate of CYP3A4; inhibits CYP1A2, 2A6, 2B6, 2C8, 2C9, 2D6, 3A4; see product labeling for numerous interactions
Monitoring	Blood pressure, assess for adverse effects
Case Notes	In the case, this African-American was started on an appropriate first-line agent for hypertension. With no compelling indications to use any particular agents over others, the provider must choose wisely. The JNC-7 Guidelines recommend choosing first from classes that have good cardiovascular prevention data such as thiazide diuretics, ACE-I, ARB, CCB, and BB. While any of these agents could be added, it must be pointed out that often the African-American population does not respond as effectively to BB, ACE-I, or ARB. This population typically has a better antihypertensive response to thiazide diuretics and CCB. So a CCB is the best choice in this case since the patient is already taking a thiazide. The DHP family of CCB is more appropriate than the non-DHP family due to the patient's chronic constipation, which could be worsened by non-DHPs. Notify PCP if leg swelling occurs. Do not confuse actions/adverse effects with non-DHP CCBs. Do not use rapid-acting DHPs, such as immediate-release nifedipine, for lowering BP (aggressively causes hypotension). Dosing for amlodipine: 2.5-10 mg once daily.

A 68-year-old female patient has been treating her hypertension with diet and exercise for one year. Over the last three months, her blood pressure has become elevated. At her last primary care provider (PCP) visit, her systolic blood pressure was elevated at 148/75 mmHg two weeks ago. He recommended she try to increase her exercise to four to five days per week. Today, she presents to her visit for follow-up on her blood pressure. She has been adherent with her therapeutic lifestyle changes. Her past medical history is significant for hypertension × one year and osteopenia × two years.

Allergies: NKDA

Medications: Calcium carbonate 600 mg plus vitamin D 125 IU tablet (OTC) 1 po once daily

Physical Exam/Other Studies:

Wt 137 lb Ht 63 in T 98.6°F BP 148/80 HR 72 RR 12 BMI 24.6

SCr 1.0 K 4.5 Clcr 119

DEXA scan (6 months ago) T-score 2.0 at wrist and ankle; 2.2 at hip

The PCP would like your help choosing an antihypertensive for this patient.

Which of the following antihypertensive medications would be most appropriate to begin at this time?

A. doxazosin
B. hydrochlorothiazide
C. aliskiren
D. furosemide

Hydrochlorothiazide (HCTZ)	Thiazide diuretics (hydrochlorothiazide, chlorothiazide, chlorthalidone, indapamide, metolazone)
Mechanism of Action	Inhibits sodium reabsorption in the distal tubule causing sodium and water excretion.
***Contraindications*/ Precautions**	*Hypersensitivity to thiazides or sulfonamides, anuria, pregnancy*/Electrolyte disturbances, hypokalemia, gout, diabetes, hepatic impairment, hypercholesterolemia, parathyroid disease, renal impairment, SLE
Adverse Effects	Orthostatic hypotension, photosensitivity, hypokalemia, anorexia, hyperuricemia. Rarely: Agranulocytosis, aplastic anemia, interstitial nephritis, Stevens-Johnson syndrome, thrombocytopenia, toxic epidermal necrolysis
Drug Interactions	Dofetilide, ACE inhibitors, analgesics, antidiabetic agents, bile acid sequestrants, calcitriol, amifostine, NSAIDs, oxcarbazepine, lithium, rituximab, topiramate
Monitoring	Fluid status, blood pressure, serum electrolytes, BUN, creatinine
Case Notes	Thiazide diuretics are considered first-line agents in the treatment of hypertension along with ACE inhibitors, ARBs, and CCBs for their efficacy in reducing CHD risk and cardiovascular morbidity and mortality. The choice of agent would depend on patient-specific compelling indications. Dosing: hydrochlorothiazide 12.5-25 mg daily; chlorothiazide 500-2,000 mg daily in 1-2 doses; chlorthalidone 25-100 mg daily, indapamide 1.25-2.5 mg daily; metolazone 2.5-5 mg daily. HCTZ is not effective in patients with a creatinine clearance < 30ml/min. Dose in the morning to avoid nocturnal enuresis. Loop diuretics like furosemide are not as effective in prevention of CHD so are not generally used in hypertension except in fluid overload states. Aliskiren is effective in the treatment of hypertension but is not considered first line. Alpha blockers like doxazosin have been shown to increase morbidity and mortality in some patients. They should be reserved for use only after other agents have been tried. They do have a role in the treatment of benign prostatic hypertrophy.

1

A 50-year-old man is seen by his physician for follow-up on his lipid panel. His medical history is significant for hypertension for five years, diabetes for five years, and hypothyroidism for 10 years. He is a smoker and only occasionally drinks alcohol. His brother had a stent placement at age 49. He has had elevated cholesterol levels in the past that have not responded to diet and exercise. His physician plans to start drug therapy at his visit today.

Allergies: NKDA

Medications: Losartan 50 mg tablet 1 po daily; plant stanol 0.7 g chewable (OTC) 1 po twice daily; levothyroxine 25 mcg tablet 1 po daily in the AM; glipizide/metformin 2.5/500 mg tablet 2 po twice daily

Physical Exam/Other Studies:

Wt 190 lb Ht 71 in T 98.6°F BP 130/85 (sitting) HR 77 RR 18 BMI 25.8

Physical exam reveals no pertinent findings.

SCr 0.8 Clcr 135 A1c 8% K 4.9 ALT 20 AST 28 TC 285 LDL 153 HDL 32 TG 500

No abnormalities were seen on ECG.

Which medication would be contraindicated in this patient?

A. HMG-CoA reductase inhibitors
B. bile acid sequestrants
C. fibric acid derivatives
D. ezetimibe

Bile Acid Sequestrants (BAS)	Cholestyramine, colestipol, colesevelam
Mechanism of Action	Binds bile acids in the intestine decreasing reabsorption, decreases enterohepatic circulation of bile acids, and increases fecal excretion of LDL-C.
***Contraindications*/ Precautions**	*Bowel obstruction, TG >500 mg/dL, history of hypertriglyceridemia-induced pancreatitis*/ Gastrointestinal disorders, TG >300 mg/dL, fat-soluble vitamin deficiencies
Adverse Effects	Constipation, bloating, epigastric fullness, nausea, flatulence, decreased absorption of fat-soluble vitamins (seen with high doses)
Drug Interactions	May decrease the absorption of multiple drugs including: warfarin, levothyroxine, thiazide diuretics, digoxin, hydrocortisone, glyburide, loop diuretics, niacin
Monitoring	Lipid panel
Case Notes	BAS predominately affect LDL, decreasing it by 15-30%. They have minimal effects on HDL, raising levels 3-5%. Bile acid sequestrants may elevate serum triglycerides, so they would be inappropriate to use in patients with hypertriglyceridemia and contraindicated in patients with triglycerides ≥500 mg/dL. Serum triglycerides ≥500 mg/dL put the patient at risk of developing acute pancreatitis. The primary goal of therapy when triglycerides are ≥500 mg/dL becomes triglyceride lowering, not LDL lowering, because of this risk. Dosing of BAS: cholestyramine (8-32 g/day); colestipol (5-30 g/day); colesevelam (3.75-4.375 g/day). Drug interactions may be reduced by separating administration times of the bile acid sequestrant from the other drug by an interval of six hours. BAS powders must be dissolved in liquid and can have a gritty texture, which may affect patient adherence. Use of the tablet dosage forms may be preferable for some patients and can improve adherence.

A 52-year-old African-American man is seen at your family medicine clinic. His medical history is significant for hypertension, which was diagnosed two years ago, and dyslipidemia diagnosed six months ago. He does not smoke and only occasionally drinks alcohol. His family history is significant for premature coronary heart disease. His brother had a stent placement at age 49. His physician has recommended a low-fat diet and exercise four to five times per week. He has been trying to control his lipids with diet and exercise for the past three months with little success.

Allergies: NKDA

Medications: Amlodipine 10 mg tablet 1 po daily; plant stanol 0.7 g chewable (OTC) 1 po twice daily

Physical Exam/Other Studies:

Wt 221 lb Ht 69 in T 98.6°F BP 144/96 sitting HR 76 RR 16 BMI 32.6

Physical exam reveals no pertinent findings.

SCr 1.0 K 4.8 ALT 20 AST 28 TC 250 LDL 185 HDL 30 TG 175

No abnormalities were seen on ECG. His Framingham risk is calculated at 17%.

Which class of medications would be most effective at lowering his LDL cholesterol level to the recommended goal?

HMG-CoA Reductase Inhibitors (statins)	Atorvastatin, fluvastatin, lovastatin, pravastatin, rosuvastatin, simvastatin
Mechanism of Action	Inhibitor of HMG-CoA reductase, which is the rate-limiting step in cholesterol synthesis. This results in a decrease in LDL cholesterol production.
***Contraindications*/ Precautions**	*Pregnancy, breast-feeding, elevated liver enzymes (>3 times the ULN), history of rhabdomyolysis*/ History of liver or renal impairment
Adverse Effects	Myalgias/arthralgias, ALT increases, CPK increases, rhabdomyolysis
Drug Interactions	CYP3A4 inhibitor (weak), CYP3A4 substrate (major), excessive ethanol consumption due to potential liver adverse effects
Monitoring	Lipid panel, LFT, CPK
Case Notes	Statins would be the best choice for this patient because they are the most effective agents at lowering total and LDL cholesterol, which are elevated in this patient, and at reducing the risk of cardiovascular disease morbidity and mortality. Dosing in this class: atorvastatin (10-80 mg/day), fluvastatin (20-80 mg/day), lovastatin (10-80 mg/day), pravastatin (10-80 mg/day), rosuvastatin (5-40 mg/day), simvastatin (5-80 mg/day). Of the statins, rosuvastatin is considered the most potent agent and fluvastatin is considered the least potent. Total cholesterol and LDL cholesterol are typically reduced by at least 30%. There is a dose-related decrease in cholesterol levels with statin therapy. Typically, doubling the dose of the statin drug will result in a 6-9% additional decrease in lipid levels. The first priority of drug therapy should be achieving LDL cholesterol goals. Response to therapy should be evaluated six weeks after starting drug therapy. Pravastatin is not metabolized by the CYP isoenzyme system and is not a potent inhibitor of that system, which may be of benefit to help reduce the risk of drug interactions.

A 45-year-old woman is seen by her physician. Her medical history is significant for Type 2 diabetes mellitus diagnosed five years ago, osteoarthritis diagnosed 1 year ago, peptic ulcer disease diagnosed 6 weeks ago, and dyslipidemia diagnosed 12 months ago. She does not smoke and only occasionally drinks alcohol. Her physician has recommended a low-fat diet and exercise four to five times per week. She has been trying to control her lipids with diet and exercise for the past six months with little success. Her physician asks your opinion regarding pharmacotherapy for her dyslipidemia.

Allergies: NKDA

Medications: Metformin/glipizide 500 mg/5 mg tablet 1 po twice daily; benazepril 10 mg tablet 1 po daily; omeprazole 20 mg tablet 1 po daily at bedtime; naproxen 500 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 184 lb Ht 66 in T 98.6°F BP 110/72 sitting HR 76 RR 18 BMI 29.7

Physical exam reveals no pertinent findings.

SCr 1.0 K 4.8 ALT 20 AST 28 TC 245 LDL 163 HDL 40 TG 210

Fasting glucose 110 A1c 6.8%

No abnormalities were seen on ECG.

What lipid-lowering medication may exacerbate this patient's pre-existing peptic ulcer disease and increase her glucose?

Niacin	No other agents in class
Mechanism of Action	Inhibits the synthesis of VLDL and LDL; also decreases the rate of catabolism of HDL.
***Contraindications*/ Precautions**	*Hypersensitivity, active hepatic disease, active peptic ulcer disease, elevated liver enzymes, arterial hemorrhage*/Unstable cardiovascular disease, diabetes, active gallbladder disease, gout, history of hepatic impairment or alcohol abuse, renal impairment
Adverse Effects	Flushing, gastrointestinal disorders, arrhythmias, diaphoresis, blurred vision, hypotension, headache, chills, dizziness, acanthosis nigricans, burning skin, hyperpigmentation, pruritus, rash, elevated liver enzymes, myalgia, CPK increases, hyperglycemia, hyperuricemia. Multiple adverse effects exist; please see prescribing information for a complete list.
Drug Interactions	HMG-CoA reductase inhibitors, bile acid sequestrants, ethanol
Monitoring	Lipid panel, LFTs, blood glucose in diabetics, CPK and serum potassium if on HMG-CoA reductase inhibitor concomitantly, uric acid if predisposed to gout, platelets and PT if on anticoagulants
Case Notes	Niacin would not be recommended in patients with active peptic ulcer disease, or pre-existing diabetes as in this case. Niacin may worsen peptic ulceration and may increase serum glucose which may result in loss of glycemic control. A more appropriate drug therapy choice would be a statin drug. Patients with well-controlled Type 2 DM are less likely to have changes in glycemic control at doses of ≤2,000 mg/day. Dosing: Immediate-release products 2,000-9,000 mg/day; sustained-release products 500-2,000 mg/day. Adverse effects of flushing and itching may be decreased by taking aspirin 325 mg shortly before the dose. Prescription sustained-release products may reduce the occurrence of adverse effects. Over-the-counter sustained-release products are not recommended as they are not more effective than immediate-release products and have an increased risk of hepatic injury.

A 58-year-old man is seen at your family medicine clinic. His medical history is significant for hypertension, which was diagnosed two years ago, dyslipidemia diagnosed six months ago, and gout diagnosed 10 years ago. He does not smoke and only occasionally drinks alcohol. His family history is significant for premature coronary heart disease. He has been treated with a statin drug for the last nine months but his LDL cholesterol is still not at recommended goals. His physician would like to add another lipid-lowering medication to his regimen and has asked for your input.

Allergies: NKDA

Medications: Amlodipine 10 mg tablet 1 po daily; plant stanol 0.7 g chewable (OTC) 1 po twice daily; simvastatin 80 mg tablet 1 po daily at bedtime; allopurinol 300 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 221 lb Ht 72 in T 98.6°F BP 148/96 sitting HR 72 RR 18 BMI 30

Physical exam reveals no pertinent findings.

ALT 25 AST 28 TC 224 LDL 145 HDL 40 TG 195

No abnormalities were seen on ECG. His Framingham risk is calculated at 17%.

Which medication could you add to his current regimen to help further lower his LDL cholesterol?

Ezetimibe	Antilipemic agent
Mechanism of Action	Inhibition of cholesterol absorption across the brush border of the small intestine decreasing cholesterol delivery to liver.
***Contraindications*/ Precautions**	*Hypersensitivity, concomitant use with a statin if active hepatic disease exists, unexplained persistent elevated transaminases, pregnancy*/History of liver or renal impairment
Adverse Effects	Myalgias/arthralgias, fatigue, diarrhea, URI, sinusitis
Drug Interactions	Increased levels of cyclosporine by ezetimibe. Ezetimibe levels may be increased by cyclosporine and may be decreased by bile acid sequestrants.
Monitoring	Lipid panel, LFT
Case Notes	Ezetimibe would add another 12-20% lowering of LDL-C for patients who are at maximum doses of other agents. It is available in a combination product with simvastatin, which may lower pill burden for patients. Other classes of lipid-lowering drugs that could be added to a statin drug to further lower LDL include: bile acid sequestrants, fibric acid derivatives, and niacin. Bile acid sequestrants may increase triglyceride levels, so they should be carefully monitored for this effect, and are prone to multiple gastrointestinal adverse effects. Additionally, they can decrease the absorption of multiple drugs. Fibric acid derivatives may also be an option; however, they are most efficacious at lowering triglycerides. Niacin has an overall favorable effect on the lipid profile but may not be appropriate in patients with gout as it may raise uric acid levels.

A 55-year-old female patient with a history of dyslipidemia is referred to you for a medication therapy recommendation. She has a history of Type 2 diabetes and is currently being treated only with diet and exercise. Her family history is significant for premature coronary artery disease. She has used lovastatin and pravastatin in the past; however, she developed severe myalgias with both agents.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily

Physical Exam/Other Studies:

Wt 221 lb Ht 72 in T 98.6°F BP 148/96 sitting HR 72 RR 18 BMI 30

Physical exam reveals no pertinent findings.

ALT 25 AST 28 TC 215 LDL 123 HDL 45 TG 350 A1c 7.5%

No abnormalities were seen on ECG.

Which medication is the best option to recommend to her provider?

A. atorvastatin
B. colesevelam
C. fenofibrate
D. ezetimibe

Fenofibrate	Fibric acid (fenofibrate, gemfibrozil)
Mechanism of Action	Peroxisome proliferator-activated receptor-alpha (PPAR-alpha) agonist that decreases VLDL and, as a result, triglyceride levels.
***Contraindications*/ Precautions**	*Hypersensitivity, hepatic dysfunction, severe renal impairment, pre-existing gallbladder disease, breast-feeding (Fenoglide only)*/Cholelithiasis—discontinue if gallstones occur, decreases in hemoglobin, hematocrit, WBC, elevated liver enzymes, liver dysfunction, rhabdomyolysis
Adverse Effects	Increases in liver function tests (LFTs), headache, abdominal pain, myalgia, constipation, nausea, CPK increases, back pain, gallstone formation, rhabdomyolysis. See prescribing information for a complete list.
Drug Interactions	Fenofibrate may increase the levels of colchicines, ezetimibe, HMG-CoA reductase inhibitors, sulfonylureas, vitamin K antagonists. Gemfibrozil may increase the levels of diabetes drugs, atorvastatin, carvedilol, colchicine, CYP1A2, 2C19, 2C9, 2C8 substrates, ezetimibe, statins, treprostinil, vitamin K antagonists. Fibric acids may decrease the levels of cyclosporine. Levels of fibric acids may be decreased by bile acid sequestrants.
Monitoring	Lipid panel, LFT, CBC
Case Notes	Although statin drugs are preferred first line for diabetic dyslipidemia, fibric acids are an acceptable alternative for patients such as this one who are unable to take statins due to adverse effects. Fibric acids have a favorable efficacy profile for diabetic patients with dyslipidemia by reducing TG and increasing HDL. Bile acid sequestrants like colesevelam could increase this patient's triglycerides and would not be the best option. Ezetimibe is unlikely to decrease her triglycerides. Dosing in this class: fenofibrate (54-201 mg/day); gemfibrozil (600-1,200 mg/day). LFTs should be monitored regularly, and fibric acids should be discontinued if the levels remain >3 times the upper limit of normal.

A 50-year-old woman with congestive heart failure is seen at her cardiologist's office for routine follow-up. In addition to heart failure, she has a medical history significant for dyslipidemia, hypertension, and osteopenia. She has daily heart failure symptoms of shortness of breath and fatigue particularly when she is active. Her symptoms have not improved despite adequate therapy with beta-blockers, ACE inhibitors, and diuretics. In the last year, she has been hospitalized once for exacerbation of her heart failure.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; lisinopril 20 mg tablet 1 po daily; metoprolol XL 100 mg tablet 1 po twice daily; furosemide 40 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 152 lb Ht 66 in T 98.6°F BP 110/78 sitting HR 75 RR 18 BNP 500 SCr 1.2 K 4.0
All other labs were within normal limits.
Echocardiogram reveals systolic dysfunction and ejection fraction of 25-30%.

Which additional medication could be added to help improve her symptoms and outcomes?

A. metolazone
B. digoxin
C. candesartan
D. spironolactone

Spironolactone	Aldosterone antagonist (spironolactone, eplerenone)
Mechanism of Action	Blockade of aldosterone that improves sodium and water excretion and reduces cardiac fibrosis and ventricular remodeling
***Contraindications*/ Precautions**	*Hypersensitivity, anuria, renal dysfunction, hyperkalemia*/Diabetes, hepatic impairment, renal impairment, electrolyte disturbances
Adverse Effects	Hyperkalemia, gynecomastia, breast pain, hypertriglyceridemia (eplerenone)
Drug Interactions	Avoid use with CYP3A4 inhibitors, ACE inhibitors, ARB, potassium supplements, NSAIDs, COX-2 inhibitors. See product information for a complete list.
Monitoring	Fluid status, renal function, potassium levels, weight, blood pressure
Case Notes	Spironolactone, an aldosterone antagonist, improves mortality in patients with class III or IV heart failure and would be a good option to add to therapy in patients not controlled on standard therapy with ACE inhibitors, beta-blockers, and diuretics. While digoxin is another agent that may improve symptoms, it does not improve mortality in heart failure. The addition of another diuretic or an ARB in addition to an ACE inhibitor will not improve outcomes. Aldosterone blockade should be considered in all patients with class III or IV heart failure or after myocardial infarction with left ventricular dysfunction to improve the mortality and decrease hospitalizations. There are no data to recommend use in patients with class I or II heart failure. The major concern with the use of these agents is the increased incidence of hyperkalemia. Therefore, aldosterone antagonists should not be used in patients with SCr >2.5 mg/dL in men or >2.0 mg/dL in women, Clcr <30 mL/min, or serum potassium level >5.0 mEq/L. Patients at risk of hyperkalemia because of medications or disease states should be monitored closely if aldosterone inhibitors are used in this group. Usual dosing in heart failure: spironolactone (12.5-25 mg/day—not much benefit is seen beyond 25 mg/day); eplerenone (25-50 mg/day).

A 65-year-old male patient with a history of dyslipidemia and hypertension for 10 years and myocardial infarction one year ago is seen by his provider for routine follow-up. The patient currently smokes approximately one pack of cigarettes a day and drinks one to two beers each evening. The patient has not had any symptom changes since his last visit. The physician notes abnormalities on examination and lab studies consistent with heart failure.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; atorvastatin 40 mg 1 po at bedtime; enalapril 10 mg 1 po twice daily

Physical Exam/Other Studies:

Wt 200 lb Ht 70 in T 98.6°F BP 128/88 sitting HR 100 RR 18 ALT 28 AST 32 TC 199 LDL 115 HDL 55 TG 145 BNP 1,200 SCr 1.4

All other labs were within normal limits.

Physical exam reveals some crackles in lung fields and S_3 gallop.

Non-specific ST-T changes on ECG.

Chest x-ray reveals cardiomegaly and edema.

Echocardiogram reveals left ventricular hypertrophy and ejection fraction of 30-35%.

Which drug class would be the most appropriate to add in this asymptomatic patient?

A. loop diuretic
B. aldosterone antagonist
C. digoxin
D. beta-blocker

Beta-Blocker	Bisoprolol, carvedilol, metoprolol succinate CR/XL
Mechanism of Action	Inhibition of beta-adrenergic receptors and alpha receptors (carvedilol) that results in a reduction in sympathetic nervous system activation. Other beneficial effects: antiarrhythmic effects, decreased ventricular remodeling, heart rate, heart wall stress, and oxygen demand.
***Contraindications*/ Precautions**	*Bradycardia or heart block, sick sinus syndrome, severe peripheral artery disease*/Atrioventricular block, bronchospastic disease, conduction abnormalities, diabetes, decompensated heart failure, hepatic impairment, peripheral vascular disease, untreated pheochromocytoma, hypotension/syncope, thyroid disease, depression, psoriasis
Adverse Effects	Hypotension, bradycardia, heart block, arterial insufficiency, dizziness, fatigue, depression, pruritus, rash, diarrhea, decrease libido, dyspnea, bronchospasm
Drug Interactions	Beta-blockers may increase the activity of alpha- and beta-agonists, alpha-blockers, antihypertensives, cardiac glycosides, phenothiazines, insulin, lidocaine, bupivacaine, methacholine, sulfonylureas. Beta-blockers may decrease the activity of $beta_2$-agonists and theophylline. Activity of beta-blockers may be affected by acetylcholinesterase inhibitors, calcium channel blockers, diazoxide, CYP2D6 inhibitors, CYP2C9 inhibitors.
Monitoring	Heart rate, blood pressure, renal function, liver function, ECG
Case Notes	The addition of a beta-blocker would be important for improving outcomes in this patient. The three beta-blockers listed have documented efficacy in improving morbidity and mortality in heart failure. Doses should be initiated low and titrated to the following target doses: bisoprolol (10 mg daily); carvedilol (25 mg po BID); metoprolol succinate CR/XL (200 mg daily). Increase doses no sooner than every two weeks to minimize intolerance or heart failure decompensation. Patients unable to tolerate target doses may be maintained at highest tolerable dose. Metoprolol succinate is the only formulation of metoprolol studied in heart failure.

A 75-year-old man with congestive heart failure for one year is seen by his physician. He has noticed an increase in his symptoms especially with walking or exertion. His medications and diet have stayed the same. In addition to heart failure, his medical history is significant for hypertension, dyslipidemia, and coronary artery disease (MI two years ago).

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; lisinopril 20 mg tablet 1 po daily; metoprolol XL 100 mg tablet 1 po twice daily; furosemide 80 mg tablet 1 po daily; spironolactone 25 mg tablet 1 po daily; nitroglycerin 0.4 mg tablet 1 sublingually as needed for chest pain

Physical Exam/Other Studies:

Wt 152 lb Ht 66 in T 98.6°F BP 110/78 sitting HR 75 RR 18 BNP 500 SCr 1.3 K 4.1 Ejection fraction 40%

Which additional medication would benefit the patient by reducing his symptoms?

A. digoxin
B. eplerenone
C. isosorbide dinitrate
D. losartan

Digoxin	Cardiac glycoside
Mechanism of Action	Inhibition of sodium/potassium ATPase pump that results in increased contractility in myocardial cells, decreases in sympathetic outflow, and decreased sodium reabsorption
***Contraindications*/ Precautions**	*Hypersensitivity, ventricular fibrillation*/Arrhythmias, acute MI, AV block, beri-beri heart disease, electrolyte imbalance, hypermetabolic states, hypertropic cardiomyopathy, renal impairment, thyroid disease, sinus nodal disease
Adverse Effects	Arrhythmias, heart block, dizziness, mental disturbances, headache, nausea, visual disturbances, diarrhea, abdominal pain
Drug Interactions	Digoxin levels are increased by: macrolide antibiotics, amiodarone, itraconazole, cyclosporine, verapamil, nefazodone, and others. Many drug interactions exist—please consult prescribing information for a complete list.
Monitoring	Heart rate, blood pressure, ECG, serum electrolytes, renal function
Case Notes	Digoxin may improve symptoms in patients who are on optimal therapy with ACE inhibitors, diuretics, beta-blockers, and aldosterone antagonists (class III and IV heart failure). Digoxin may be especially useful in the patient with heart failure that develops atrial fibrillation. Digoxin does not improve morbidity or mortality in heart failure. The optimal dose of digoxin in heart failure is 0.125-0.25 mg/day. Target serum concentrations are 0.5-1.0 ng/dL. Digoxin has a narrow therapeutic index, so patients at risk of toxicity or exhibiting signs or symptoms of toxicity should have serum blood levels checked. Digoxin is also used for rate control in patients with atrial fibrillation.

A 70-year-old female patient with a history of dyslipidemia and hypertension for 15+ years has been treated for heart failure for the last six months. She was admitted to the hospital for an acute exacerbation of her heart failure. IV diuretics and IV nitroglycerin were started two days ago and her symptoms and urine output improved, but now she has had a drop in blood pressure, and her serum creatinine has risen from 1.1 to 3.5 mg/dL. A Swan-Ganz catheter is placed for hemodynamic monitoring.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; enalapril 10 mg tablet 1 po twice daily; carvedilol 6.25 mg tablet 1 po twice daily; digoxin 0.125 mg tablet 1 po daily; furosemide 120 mg IV twice daily; metolazone 2.5 mg tablet 1 po daily; nitroglycerin IV infusion 10 mcg/min

Physical Exam/Other Studies:

Physical exam reveals cold and cyanotic extremities.

Wt 162 lb Ht 62 in T 98.6°F BP 110/68 sitting HR 75 RR 18

ALT 35 AST 38 BNP 2,000 SCr 3.5 BUN 40 CI 1.2 PAOP 32

What therapy should be added at this time?

Inotropes	Dobutamine, milrinone
Mechanism of Action	Dobutamine is a beta$_1$ agonist, and milrinone is a phosphodiesterase inhibitor. Both increase cAMP, which increases cardiac output and decrease systemic vascular resistance.
***Contraindications*/Precautions**	*Hypersensitivity, idiopathic subaortic stenosis*/Hypotension, hypertension, hypovolemia, myocardial infarction, MAO inhibitor use (dobutamine), arrhythmias, hepatic changes, aortic stenosis, electrolyte imbalance, myocardial infarction, thrombocytopenia (milrinone)
Adverse Effects	Increased blood pressure, tachycardia, hypotension, arrhythmias. For a complete list, see package insert for individual agents.
Drug Interactions	Dobutamine may increase the effects of sympathomimetics. Levels of dobutamine may be decreased by calcium salts.
Monitoring	Blood pressure, ECG, heart rate, CVP, MAP, RAP, urine output, CI, PAOP, SVR, platelet count, CBC, electrolytes, liver and renal function
Case Notes	Inotropic therapy is recommended in patients with diminished peripheral perfusion or end-organ dysfunction to improve symptoms and output. These agents may be useful particularly in the following situations: systolic blood pressure < 90 mm Hg; symptomatic hypotension despite normal filling pressures; no response or poor response to IV vasodilators; fluid overload with poor response to IV diuretics; or worsening renal function with fluid overload. Routine use of milrinone in acute exacerbations of heart failure is not recommended secondary to lack of mortality benefit. Dobutamine is the inotrope of choice especially in hypotensive patients. Milrinone is the inotrope of choice in patients receiving a beta-blocker.

A 70-year-old female patient with a history of dyslipidemia and hypertension for 15+ years is seen by her primary care physician for increased symptoms of shortness of breath and fatigue in her daily activities. She notices her symptoms are worse when she walks up stairs. She currently smokes one to two cigarettes per day and does not drink alcohol.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily, simvastatin 40 mg tablet 1 po at bedtime; enalapril 10 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Physical exam reveals crackles in both lung fields, S_3 gallop, 2+ pitting edema bilaterally, and jugular venous distension.
Wt 152 lb Ht 62 in T 98.6°F BP 128/88 sitting HR 100-130 RR 18
ALT 25 AST 28 TC 168 LDL 85 HDL 55 TG 140 BNP 1,100 SCr 1.2
All other labs were within normal limits.
Nonspecific ST-T changes on ECG.
Chest x-ray reveals cardiomegaly and edema.
Echocardiogram reveals systolic dysfunction and ejection fraction of 35-40%.

After completing her physical exam and reviewing her lab work, her physician diagnoses her with heart failure. The physician begins carvedilol 3.125 mg 1 po twice daily.

Which additional medication would benefit the patient by reducing her symptoms?

A. furosemide
B. spironolactone
C. hydralazine
D. losartan

Furosemide	Loop diuretic (furosemide, bumetanide, torsemide, ethacrynic acid)
Mechanism of Action	Inhibition of sodium and chloride reabsorption in the ascending loop of Henle and distal renal tubule resulting in the excretion of water, sodium, chloride, magnesium, and calcium
***Contraindications*/ Precautions**	*Hypersensitivity, anuria*/Fluid and electrolyte loss, nephrotoxicity, sulfonamide allergy (except ethacrynic acid)
Adverse Effects	Dehydration, dizziness, hypotension, renal dysfunction, gout, hyperglycemia, electrolyte disturbances, ototoxicity, jaundice, hematologic effects, photosensitivity. For a complete list, see prescribing information.
Drug Interactions	Loop diuretics may increase the effects/toxicities of: ACE inhibitors, allopurinol, amifostine, aminoglycosides, antihypertensives, cisplatin, dofetilide, hypotensive agents, lithium, salicylates
Monitoring	Fluid status, blood pressure, orthostasis, serum electrolytes, renal function, hearing
Case Notes	First-line agents in the treatment of congestive heart failure include ACE inhibitors and beta-blockers. Diuretics are a good addition to patients who are symptomatic due to fluid retention. Diuretics do not improve mortality from heart failure but are effective at improving patient quality of life. Optimal dosing of loop diuretics in heart failure: furosemide 80-160 mg/day; bumetanide 1-2 mg/day; torsemide 20-40 mg/day, ethacrynic acid 50-200 mg/day. Dosing beyond this dose is unlikely to improve diuresis. In patients requiring additional diuresis, increasing the frequency of dosing is most effective. The appropriate maintenance dosing is the dose that maintains the patient at a stable weight without edema and other symptoms of fluid retention. Patients should monitor weight daily, and increases of 3-5 pounds over a week would necessitate the increase in diuretic therapy. Loop diuretics are capable of causing ototoxicity especially with IV administration. Equally important in the treatment of heart failure is smoking cessation, so it would be important to advise the patient to quit and assist her in that attempt.

A 70-year-old female patient with a history of dyslipidemia and hypertension for 15+ years has been treated for heart failure for the last six months. She presented to the emergency room 48 hours ago with worsening of her symptoms. She has increasing dyspnea, orthopnea, and lower extremity edema. She has had about a 20-lb weight gain over the last two weeks. She had changed her diet lately and was eating out or eating pre-made meals more often (five nights/week). She is admitted to the hospital for acute decompensated heart failure, and her diuretic regimen is changed. Despite increased diuretic use, she has had minimal increases in urine output, and little change in her symptoms.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; enalapril 10 mg tablet 1 po twice daily; carvedilol 6.25 mg tablet 1 po twice daily; digoxin 0.125 mg tablet 1 po daily; furosemide 120 mg IV twice daily; metolazone 2.5 mg tablet 1 po once daily

Physical Exam/Other Studies:

Physical exam reveals crackles in both lung fields, S_3 gallop, 3+ pitting edema bilaterally, and jugular venous distension.

Wt 162 lb Ht 62 in T 98.6°F BP 110/68 sitting HR 75 RR 18

ALT 35 AST 38 BNP 2,000 SCr 1.1 BUN 25 Clcr 52

All other labs were within normal limits.

Which therapy should be added at this time?

IV Vasodilators	Sodium nitroprusside, nesiritide, nitroglycerin
Mechanism of Action	Vasodilation, which helps reduce congestion and improve renal perfusion and output in the patient with fluid overload
***Contraindications*/ Precautions**	*Hypersensitivity, renal insufficiency (nitroprusside)*/Hypotension, renal impairment. Contraindications and precautions vary with individual agent. Please consult prescribing information for each agent.
Adverse Effects	Hypotension, tachycardia, increased serum creatinine (nesiritide), cyanide toxicity (sodium nitroprusside). For a complete list, see prescribing information for individual agents.
Drug Interactions	Hypotensive agents, phosphodiesterase-5 inhibitors (nitroglycerin—avoid use)
Monitoring	Symptoms, fluid status, blood pressure, renal function, hemodynamic response, cyanide and thiocyanate toxicity (sodium nitroprusside)
Case Notes	IV vasodilators may be used in addition to IV loop diuretics for patients with an exacerbation of heart failure to improve symptoms. Sodium nitroprusside typically is administered in a dose of 0.5-1 mcg/kg/min. Patients with severe renal impairment should not receive sodium nitroprusside because of the increased risk of cyanide toxicity. Rebound worsening may occur if sodium nitroprusside is stopped abruptly; doses should be tapered down before discontinuing. Nesiritide is a recombinant B-type natriuretic peptide that is typically dosed as 0.01 mcg/kg/min following an IV bolus of 2 mcg/kg. Nitroglycerin is dosed as 25-75 mcg/min titrated to response. Nitroglycerin and nesiritide provide similar benefits to the patient. Nesiritide use may result in increased serum creatinine levels and decreased glomerular filtration. Nitroglycerin use may result in tachyphylaxis and reflex tachycardia.

A 75-year-old female patient is status post hip replacement eight days ago. She is still unable to ambulate well. Her nurses have noticed that she has had a drop in her platelet count. She is short of breath and has inspiratory chest pain.

Allergies: Penicillin (rash)

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; enalapril 10 mg tablet 1 po daily; prednisone 5 mg tablet 1 po daily, enoxaparin 30 mg/0.3 mL subcutaneous injection given every 12 hours

Physical Exam/Other Studies:

Wt 182 lb Ht 63 in T 98.6°F BP 128/78 sitting HR 77 RR 18

TC 178 LDL 95 HDL 55 TG 140 SCr 0.9 INR 2.1 PLT 120×10^3

(Post-op Day 2 227×10^3)

Physical exam reveals clear lungs with no wheezes or crackles.

CT angiography is consistent with pulmonary embolism.

HIPA assay and heparin-PF4 ELISA assay are positive.

The hospitalist on duty diagnoses her with heparin-induced thrombocytopenia (HIT).

What options are available to manage her HIT?

Direct Thrombin Inhibitors	Lepirudin, argatroban, bivalirudin
Mechanism of Action	Direct inhibition of thrombin preventing thrombus formation
***Contraindications*/ Precautions**	*Hypersensitivity*/Bleeding, hepatic impairment, renal impairment
Adverse Effects	Bleeding risk, thrombocytopenia
Drug Interactions	Thrombolytic agents, anticoagulants
Monitoring	aPTT, hemoglobin, hematocrit
Case Notes	Heparin-induced thrombocytopenia (HIT) is an uncommon but potentially life-threatening complication of heparin therapy. It should be suspected in the following conditions: the patient has had a drop in platelet count of >50% from baseline or to <150,000; it is day five or greater of heparin therapy; other causes of thrombocytopenia have been ruled out. Direct thrombin inhibitors are the drugs of choice for treating HIT. The anti-factor Xa inhibitor fondaparinux has also been used in the treatment of the disorder. All forms of heparin should be discontinued immediately when HIT is suspected, and one of these alternative anticoagulants should be initiated. Dosing varies by agent. When the platelet count is at least ≥100,000 or preferably ≥150,000, warfarin therapy should be initiated as well and should be overlapped with the direct thrombin inhibitor for at least two days with therapeutic INR >2. If the patient was on warfarin therapy when the HIT occurred, it should be discontinued and vitamin K (5-10 mg oral or IV) should be administered. The warfarin should be withheld until platelet counts recover to at least 100,000. Doses of lepirudin and bivalirudin should be adjusted in renal impairment, and argatroban doses should be adjusted in hepatic impairment. Direct thrombin inhibitors are also alternatives for VTE prophylaxis or treatment and in the treatment of ACS in patients with a history of HIT. One investigational oral direct thrombin inhibitor dabigatran is being used in the prevention of stroke in atrial fibrillation and for prevention and treatment of VTE.

A 75-year-old female patient with a history of temporal neuralgia, hypertension, dyslipidemia, and osteopenia develops avascular necrosis of her left hip and is scheduled for hip replacement surgery.

Allergies: Penicillin (rash)

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; calcium citrate 600 mg tablet (OTC) 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; enalapril 10 mg tablet 1 po daily; prednisone 5 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 182 lb Ht 63 in T 98.6°F BP 128/78 sitting HR 77 RR 18

TC 178 LDL 95 HDL 55 TG 140 SCr 0.9

All other labs were within normal limits.

On the day after her surgery, her surgeon would like to begin venous thromboembolism (VTE) prophylaxis with a low molecular weight heparin (LMWH). Which of the following would be considered an appropriate agent?

A. fondaparinux
B. enoxaparin
C. argatroban
D. bivalirudin

Enoxaparin	Low molecular weight heparin (enoxaparin, dalteparin, tinzaparin)
Mechanism of Action	Inhibition of factor Xa preventing thrombus formation and growth
***Contraindications*/ Precautions**	*Hypersensitivity to heparin or LMWH, pork allergy, heparin-induced thrombocytopenia, active bleeding, severe liver disease, malignant hypertension, platelet count <20,000*/Spinal or epidural anesthesia, bleeding, hyperkalemia, history of heparin-induced thrombocytopenia, prosthetic heart valves, renal failure Clcr <30 mL/min.
Adverse Effects	Bleeding risk, thrombocytopenia
Drug Interactions	Antiplatelets, anticoagulants, NSAIDs
Monitoring	Anti-Xa levels, baseline PT/INR, aPTT, CBC, platelets, SCr
Case Notes	In this case, the only low molecular weight heparin option listed was enoxaparin. LMWH and unfractionated heparin (UFH) are commonly used agents for venous thromboembolism (VTE) prophylaxis and treatment. Other anticoagulants such as anti-Xa inhibitors (fondaparinux), direct thrombin inhibitors (argatroban and bivalirudin), and warfarin may also be used to prevent or treat venous thromboembolism. Fondaparinux is effective at VTE prevention, although it may not be preferable over LMWH due to concerns regarding bleeding risks. Argatroban and bivalirudin do not have an indication for VTE prophylaxis at this time. LMWH may be preferable over unfractionated heparin due to: the predictable dose response when compared to UFH, improved subcutaneous bioavailability, longer half-life, lower incidence of thrombocytopenia, dose-dependent clearance, and reduced monitoring. LMWH are also relatively safe to use for long-term anticoagulation during pregnancy. All LMWH are administered via subcutaneous injection. Dosing of LMWH varies with indication. Anti-Xa levels may be used for monitoring (0.5-1.0 units/mL target for treatment of VTE and 0.2-0.4 units/mL target for prevention of VTE).

A 25-year-old woman presents to the emergency room with complaints of shortness of breath and dyspnea. She is experiencing chest tightness and pain with inspiration. Her symptoms began earlier in the day and have gradually worsened, and she is now experiencing dizziness and lightheadedness.

Allergies: NKDA

Medications: Combined oral contraceptive tablets 1 po daily

Physical Exam/Other Studies:

Wt 122 lb Ht 66 in T 98.6°F BP 110/78 sitting HR 77 RR 18 SCr 0.9

Chest x-ray shows nonspecific infiltrates in the right lobe of the lungs. CT angiography and D-dimer results are consistent with pulmonary embolism.

She is diagnosed with a pulmonary embolism.

Which of the following would be an appropriate treatment for pulmonary embolism (PE)?

A. unfractionated heparin
B. aspirin
C. argatroban
D. clopidogrel

Unfractionated Heparin (UFH)	Heparins (no other unfractionated heparins in class)
Mechanism of Action	Binds to and potentiates the actions of antithrombin III, which inactivates thrombin and clotting factors IX, X, XI, XII and plasmin resulting in anticoagulation
***Contraindications*/ Precautions**	*Hypersensitivity to heparin, heparin-induced thrombocytopenia, active bleeding, severe liver disease, malignant hypertension, platelet count <20,000, disseminated intravascular coagulation, suspected intracranial hemorrhage*/Bleeding, hyperkalemia, history of heparin-induced thrombocytopenia, heparin resistance, hyperkalemia, osteoporosis
Adverse Effects	Bleeding, thrombocytopenia
Drug Interactions	Antiplatelets, anticoagulants, NSAIDs
Monitoring	Hemoglobin, hematocrit, signs of bleeding, aPTT or ACT, anti-Xa levels, platelets
Case Notes	Low molecular weight heparins and unfractionated heparin (UFH) are commonly used agents for treatment of venous thromboembolism (VTE). UFH requires frequent monitoring because of an unpredictable response. Activated clotting time or aPTT may be used to monitor heparin. Typically the therapeutic range is 1.5-2.5 times control. However, anti-Xa levels are becoming the preferred lab for monitoring (target 0.3-0.7 units/mL). Initial loading dose of heparin for the treatment of VTE is 80-100 units/kg followed by an initial infusion rate of 17-20 units/kg/h. The dose is then adjusted based on aPTT or ACT. Heparin may also be dosed subcutaneously at a dose of 17,500 units or 250 units/kg then 250 units/kg every 12 hours. Dosage adjustments are then made by anti-Xa levels. Heparin-induced thrombocytopenia is a rare but life-threatening complication of heparin use. Both unfractionated and low molecular weight heparins are safe to use during pregnancy. Protamine is an agent that is used to reverse the effects of heparin related to overdose or in patients who develop bleeding complications. The dose is based on the amount of heparin administered and the time elapsed since administration.

A 65-year-old man presents to the emergency room with complaints of abnormal heart rate. He has had what he describes as a "racing heart beat" and shortness of breath and dizziness for about the last 24 hours. He has a medical history that is significant for hypertension. He currently smokes half of a pack of cigarettes per day and does not drink alcohol.

Allergies: NKDA

Medications: Benazepril 10 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 182 lb Ht 71 in T 98.6°F BP 140/90 sitting HR 140 RR 18 SCr 1.2

All other labs were within normal limits.

ECG shows irregularly irregular ventricular rate with the absence of P waves consistent with atrial fibrillation.

Which medication would be best to control this patient's rapid heart rate?

A. digoxin
B. diltiazem
C. amiodarone
D. lidocaine

Diltiazem	Calcium channel blocker—nondihydropyridine (diltiazem, verapamil)
Mechanism of Action	Inhibition of calcium entry into areas of the smooth muscle and myocardium, which results in decreased heart rate, decreased ventricular contractility, and prolongation of the P-R interval
***Contraindications*/ Precautions**	*Hypersensitivity, sick sinus syndrome, second- or third-degree AV block, severe hypotension, pulmonary congestion, acute MI, cardiogenic shock, recent IV beta-blocker use, Wolff-Parkinson-White syndrome*/ Conduction abnormalities, muscular dystrophy, erythema multiforme or exfoliative dermatitis, liver enzyme changes, hypotension/syncope, peripheral edema, obstructive cardiomyopathy, left ventricular dysfunction, renal impairment
Adverse Effects	Bradycardia, heart block, edema, headache, dizziness, constipation, rhinitis, gingival hyperplasia
Drug Interactions	Avoid concomitant use with dabigatran, disopyramide, dofetilide, topotecan, tolvaptan. Multiple drug interactions exist for each agent, see prescribing information for complete list.
Monitoring	Blood pressure, heart rate, ECG
Case Notes	Control of ventricular rate and symptoms would be the treatment goals for a patient in an episode of atrial fibrillation. An IV calcium channel blocker would be one option for rate control of this episode of atrial fibrillation. Other agents that can also be used include IV beta-blockers and IV digoxin. IV digoxin is not recommended for first-line therapy unless the patient is experiencing heart failure or left ventricular dysfunction. Amiodarone may be used in atrial fibrillation to control the abnormal rhythm after the rate control has been established. Lidocaine is not useful in the treatment of atrial fibrillation. Both calcium channel blockers and beta-blockers are useful in atrial fibrillation. Beta-blockers are more effective than calcium channel blockers at rate control. However, calcium channel blockers may be preferable in patients with respiratory disease. The goal of rate control should be to control the resting heart rate to <80 and the exercise heart rate to <100.

A 65-year-old male patient presented to the emergency room with complaints of abnormal heart rate four days ago. He was diagnosed with atrial fibrillation, admitted to the hospital, given intravenous diltiazem to control his ventricular rate, and started on oral diltiazem. He has a medical history that is significant for hypertension. He currently smokes half of a pack of cigarettes per day and does not drink alcohol.

Allergies: NKDA

Medications: Diltiazem XR 120 mg capsule 1 po once daily

Physical Exam/Other Studies:

Wt 182 lb Ht 71 in T 98.6°F BP 140/90 sitting HR 78 RR 18 SCr 1.0

All other labs were within normal limits.

ECG shows irregularly irregular rhythm of atrial fibrillation.

This patient's heart rate is controlled, and he is being discharged. His cardiologist is starting him on anticoagulation therapy to decrease the risk of stroke.

Which is the best anticoagulant option for this patient?

A. aspirin C. aspirin and warfarin

B. warfarin D. bivalirudin

Warfarin	Vitamin K antagonist (no other agents in class)
Mechanism of Action	Depletion of functional vitamin K reserves resulting in reduced synthesis of active clotting factors (II, VII, IX, X) and proteins C and S
***Contraindications*/ Precautions**	*Hypersensitivity, bleeding risk, aneurysm, hemorrhage, malignant hypertension, alcoholism, pregnancy, subacute bacterial endocarditis, history of warfarin-induced necrosis, pericarditis, pericardial effusion*/High risk of bleeding, skin necrosis/gangrene, purple toe syndrome, dietary insufficiency, heparin-induced thrombocytopenia, hepatic impairment, infection, renal impairment, thyroid disease. Multiple warnings/precautions exist—consult product information.
Adverse Effects	Bleeding is the major adverse effect. Consult product information for other possible adverse effects.
Drug Interactions	Substrate of CYP1A2, 2C9, 2C19, 3A4. Avoid concomitant use with anticoagulants/antiplatelet agents, tamoxifen.
Monitoring	INR, prothrombin time, hematocrit, signs and symptoms of bleeding/thrombosis. Consider genotyping prior to therapy for CYP2C9 and VKORC1.
Case Notes	Aspirin and warfarin both may be used for anticoagulation in patients with atrial fibrillation. Bivalirudin is not indicated for this use. The choice of agent depends on the patient's risk factors for stroke. Patients at high risk: prior stroke, transient ischemic attack or embolus, mitral valve disease, or prosthetic valves should use warfarin (INR goal 2-3). Patients at moderate risk: hypertension, heart failure, left ventricular dysfunction, age >75 years, diabetes may use aspirin 81-325 mg or warfarin (INR goal 2-3). Patients with no risk factors at low risk (<65 years of age and no cardiovascular disease or diabetes) may use aspirin 81-325 mg. Chronic warfarin therapy is also routinely used for prevention and treatment of other thromboembolic disorders such as DVT and PE.

A 65-year-old male patient presented to the emergency room with complaints of abnormal heart rate four days ago. He was diagnosed with atrial fibrillation and given IV diltiazem to control his ventricular rate and was started on oral diltiazem. He has a medical history that is significant for hypertension. He currently smokes half of a pack of cigarettes per day and does not drink alcohol.

Allergies: NKDA

Medications: Diltiazem XR 120 mg capsule 1 po once daily;

Physical Exam/Other Studies:

Wt 182 lb Ht 71 in T 98.6°F BP 140/90 sitting HR 78 RR 18 SCr 1.0

All other labs were within normal limits.

ECG shows irregularly irregular rhythm of atrial fibrillation.

This patient's heart rate is controlled, and he is being discharged. His cardiologist would like to try cardioversion since this is an isolated episode. Anticoagulation with warfarin is started, and he is scheduled for cardioversion in one month.

Which of the following may be used for cardioversion in a patient with atrial fibrillation?

A. amiodarone C. verapamil
B. quinidine D. lidocaine

Amiodarone	Antiarrhythmic drug (Class III: amiodarone, dronedarone, ibutilide, dofetilide)
Mechanism of Action	Inhibits adrenergic stimulation; blocks potassium, calcium, and sodium channels; delays repolarization of the myocardial tissue; decreases AV conduction
***Contraindications*/ Precautions**	*Hypersensitivity, sinus node dysfunction, second- and third-degree heart block, bradycardia, cardiogenic shock*/Arrhythmias, hepatotoxicity, pulmonary toxicity, optic neuritis/neuropathy, photosensitivity, electrolyte imbalances, thyroid disease, drugs that cause QT_c prolongation
Adverse Effects	Thyroid disease, skin abnormalities, neurologic disorders, arrhythmias, pulmonary toxicities, gastrointestinal disorders, hepatic disorders, ocular disorders. Multiple adverse reactions exist—consult prescribing information.
Drug Interactions	Inhibits CYP2A6, 2C9, 3A4, 2D6; substrate for CYP2C8, 3A4
Monitoring	Blood pressure, heart rate, ECG, chest x-ray, pulmonary function tests, liver function tests, thyroid function tests, ophthalmic exams, check for lethargy, edema of hands or feet, or weight loss
Case Notes	Amiodarone is one agent that may be used to chemically convert patients with atrial fibrillation back to normal sinus rhythm. Other antiarrhythmic drugs that may be used include other type III agents, ibutilide and dofetilide, and the 1c agents flecainide and propafenone. Pharmacologic cardioversion is most effective when completed within seven days of onset of atrial fibrillation. If ventricular rate control is established, cardioversion with drugs or DCC is not required to control the atrial fibrillation. Rate control and rhythm control (if necessary to control symptoms) may be the best options for the long-term treatment of the patient. If cardioversion is performed, the patient must be adequately anticoagulated prior to the attempt if the duration of the atrial fibrillation exceeds 48 hours or is unknown. Warfarin is the agent of choice for anticoagulation and must be given for at least three weeks prior to and four weeks after cardioversion.

A 42-year-old woman presents to the emergency room with 8/10 substernal chest pain and pressure radiating into her jaw that has been occurring for the last 12 hours. She has a history of coronary artery disease, hypertension, and dyslipidemia.

Allergies: NKDA

Medications: Metoprolol 50 mg tablet 1 po twice daily; atorvastatin 80 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; nitroglycerin 0.4 mg tablet 1 sublingually every 5 minutes for angina

Physical Exam/Other Studies:

Wt 150 lb Ht 66 in T 98.6°F BP 160/98 HR 100 RR 18 BMI 24.2

SCr 1.4 TC 180 LDL 88 HDL 55 TG 185 CK 300 CK-MB 25 Troponin I 0.8

ECG shows changes consistent with NSTEMI.

A diagnosis of non-ST segment elevation myocardial infarction (NSTEMI) is made. Morphine, oxygen, heparin, and metoprolol are begun.

It is planned to send the patient to the cardiac catheterization lab for PCI and stent placement. Two-vessel disease is found, and stents are placed in both arteries.

Which of the following therapies should be added to her medication regimen to prevent restenosis and thrombosis related to stent placement?

A. heparin C. clopidogrel

B. warfarin D. dipyridamole

Clopidogrel	Antiplatelets (aspirin, clopidogrel, prasugrel, ticlopidine, dipyridamole)
Mechanism of Action	Inhibition of platelet aggregation and thrombus formation; vasodilation (dipyridamole)
***Contraindications*/ Precautions**	*Hypersensitivity, bleeding disorders, children, hematopoietic disorders*/Risk of bleeding, thrombotic thrombocytopenic purpura, hepatic impairment, renal impairment, concurrent use of CYP2C19 inhibitors such as PPIs, poor metabolizers of CYP2C19, gastrointestinal disease, heavy ethanol use, concurrent NSAID/COX-2 inhibitor use, patients ≥75 years of age
Adverse Effects	Bleeding, nausea, vomiting, dyspepsia, gastrointestinal ulcers/erosions, anemia, rash, neutropenia (ticlopidine)
Drug Interactions	NSAIDs, CPY2C19 substrate (clopidogrel), methotrexate, anticoagulants. Multiple interactions exist; please consult prescribing information.
Monitoring	Signs/symptoms of bleeding or thrombosis, hemoglobin, hematocrit, CBC (ticlopidine)
Case Notes	Dual antiplatelet therapy with clopidogrel or prasugrel and aspirin for patients receiving PCI plus stent placement has been proven to reduce the occurrence of restenosis and stent thrombosis. Heparin is not recommended post-stent placement to prevent these complications. Warfarin and dipyridamole are not recommended for use in this situation either. Typically, therapies are begun prior to the procedure in the following doses: ASA (75-325 mg) and clopidogrel (300-600 mg at least six hours prior). For bare metal stent placement, dual antiplatelet therapy should be continued for a minimum of one month and ideally up to one year. For drug-eluting stents, the dual antiplatelet therapy should be continued for one year minimum. Dual antiplatelet therapy for one year is also an option for patients with NSTEMI acute coronary syndromes and unstable angina who do not undergo PCI/stent placement. Ticlopidine is not recommended because of its lack of superiority over clopidogrel and unfavorable side effect profile. Prasugrel may be used in place of clopidogrel in patients who may be considered to be poor metabolizers of clopidogrel.

A 42-year-old woman presents to the emergency room with 8/10 substernal chest pain and pressure radiating into her jaw that has been occurring for the last 12 hours. She has a history of coronary artery disease, hypertension, and dyslipidemia.

Allergies: NKDA

Medications: Metoprolol 50 mg tablet 1 po twice daily; atorvastatin 80 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; nitroglycerin 0.4 mg tablet 1 sublingually every 5 minutes for angina

Physical Exam/Other Studies:

Wt 150 lb Ht 66 in T 98.6°F BP 160/98 HR 100 RR 18 BMI 24.2
SCr 1.4 TC 180 LDL 88 HDL 55 TG 185 CK 300 CK-MB 25 Troponin I 0.8
ECG shows changes consistent with NSTEMI.

A diagnosis of non-ST segment elevation myocardial infarction (NSTEMI) is made.
She is taken to the cardiac catheterization lab. PCI and stent placement are planned for two-vessel disease. Before the procedure, aspirin 325 mg po × 1 and clopidogrel 600 mg po × 1 are given, and IV heparin is started.

In addition to these antiplatelet agents, what other agents should be given prior to the intervention?

Glycoprotein IIb/IIIa Receptor Antagonists	Abciximab, eptifibatide, tirofiban
Mechanism of Action	Binds to IIb/IIIa receptors on the platelet, inhibiting aggregation
***Contraindications*/ Precautions**	*Hypersensitivity, active internal hemorrhage, history of cerebrovascular accident within two years, oral anticoagulant administration, bleeding abnormalities, thrombocytopenia, recent surgery, intracranial tumor, arteriovenous malformation or aneurysm, severe uncontrolled hypertension, history of vasculitis, use of dextran prior to PTCA*/Bleeding risks, thrombocytopenia
Adverse Effects	Bleeding, thrombocytopenia, coronary artery dissection, hypotension, nausea, back pain
Drug Interactions	Dextran (abciximab), anticoagulants, antiplatelets, drotrecogin alfa, thrombolytic agents
Monitoring	Signs/symptoms of bleeding, PT/aPTT, ACT, platelet count
Case Notes	Glycoprotein IIb/IIIa inhibitors, when administered IV prior to and during PCI, reduce the risk of MI, repeat PCI, and death. These agents are given in addition to other antiplatelet and anticoagulant therapies. Depending on when these agents are begun (prior to cardiac catheterization or post catheterization prior to PCI), one agent may be recommended over another. Eptifibatide and tirofiban are renally eliminated so the dosages should be adjusted in renal impairment. The indications for these agents are NSTEMI/STEMI and PCI. If they are given to patients receiving thrombolytic therapy, the dose must be reduced by half.

A 52-year-old African-American man is diagnosed with coronary artery disease and chronic stable angina. He experiences substernal chest pain with emotion or physical exertion that subsides with rest. His medical history is significant for hypertension × 12 years and dyslipidemia × 10 years. He currently smokes half of a pack of cigarettes/day and drinks one to two drinks/night.

Allergies: NKDA

Medications: Atenolol 50 mg tablet 1 po daily; atorvastatin 40 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 250 lb Ht 71 in T 98.6°F BP 130/78 sitting HR 76 RR 18 BMI 34.9

Physical exam reveals no pertinent findings.

SCr 0.9 TC 190 LDL 108 HDL 45 TG 185

No abnormalities were seen on ECG—no evidence of previous MI on ECG.

Exercise tolerance test was abnormal, suggesting ischemic heart disease.

Which class of medications may be added to this regimen to help reduce acute angina symptoms?

Nitrates	Nitroglycerin (sublingual, oral, topical), isosorbide dinitrate (sublingual, oral), isosorbide mononitrate (oral)
Mechanism of Action	Venous and arterial vasodilation resulting in decreased myocardial oxygen demand, decreased preload from left ventricular end diastolic volume and pressure
***Contraindications*/ Precautions**	*Hypersensitivity, concurrent use of phosphodiesterase-5 inhibitors, angle closure glaucoma, severe anemia, head trauma or cerebral hemorrhage*/Hypotension, hypertrophic cardiomyopathy, tolerance, sound alike/look alike medications
Adverse Effects	Headache, hypotension, nausea, vomiting, weakness, dizziness, blurred vision, diaphoresis, syncope
Drug Interactions	Phosphodiesterase-5 inhibitors, hypotensive agents, rosiglitazone, CYP3A4 substrate
Monitoring	Effectiveness, tolerance to nitrate
Case Notes	Nitrates can be added to other therapies to manage anginal symptoms. Sublingual nitroglycerin dosed 0.2 mg to 0.6 mg every five minutes for a maximum of three doses is useful in patients to reduce infrequent angina symptoms. For patients who have at least daily symptoms, chronic prophylactic therapy with oral or topical nitroglycerin, isosorbide dinitrate, or isosorbide mononitrate may be effective to reduce symptoms. Daily nitrate therapy is appropriate in patients who have symptoms despite treatment with beta-blockers and calcium channel blockers. However, there is controversy around the benefit provided by chronic daily nitrate therapy. The development of tolerance happens with all daily nitrate therapies in as little as 24 hours of use. Patients should have a nitrate-free interval of at least 8 to 12 hours to minimize tolerance. No dosage form of any nitrate product is free from the development of tolerance or more efficacious in the prevention of angina symptoms.

A 66-year-old man presents to the emergency room with 10/10 substernal chest pain, and pressure radiating into his jaw that has been occurring for the last six hours. He has a history of coronary artery disease, hypertension, diabetes, and dyslipidemia.

Allergies: NKDA

Medications: Metoprolol 50 mg tablet 1 po twice daily; atorvastatin 80 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; nitroglycerin 0.4 mg tablet 1 sublingually every five minutes for angina; metformin 1,000 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 193 lb Ht 70 in T 98.6°F BP 170/99 HR 100 RR 22
SCr 1.3 TC 190 LDL 98 HDL 55 TG 185 CK 350 A1c 8.2 CK-MB 45
Troponin-I 1.0
ECG shows 3-mm ST segment elevation.

A diagnosis of ST segment elevation myocardial infarction (STEMI) is made. The hospital does not have a coronary catheterization laboratory.

What type of medication therapy may be used for management of this patient's myocardial infarction?

Thrombolytics	Streptokinase, alteplase (t-PA), reteplase (r-PA), tenecteplase (TNK)
Mechanism of Action	Initiates fibrinolysis within the clot to restore blood flow to the occluded area.
***Contraindications*/ Precautions**	*Hypersensitivity, intracranial tumor, prior intracranial hemorrhage, head/facial trauma within three months, suspected aortic dissection, ischemic stroke within three months except ischemic stroke within three hours, active internal bleeding or bleeding diathesis*/Blood pressure >180/110, chronic, severe, poorly controlled hypertension, prior ischemic stroke >3 months, dementia, puncture of a noncompressible vessel, cardiopulmonary resuscitation for >10 minutes, major surgery <3 weeks, recent internal bleeding within 24 weeks, active peptic ulcer, current use of anticoagulant (INR 2-3 on warfarin), pregnancy, prior streptokinase exposure >5 days
Adverse Effects	Stroke (intracerebral hemorrhage), hemorrhage, hematoma formation, bleeding
Drug Interactions	Anticoagulants, drotrecogin alfa, antiplatelet agents, NSAIDs
Monitoring	Signs/symptoms of bleeding, neurologic assessments, blood pressure, ECG
Case Notes	Thrombolytic therapy is an option for the management of STEMI. The benefit of thrombolytic therapy depends on the time to administration. Practice guidelines recommend that thrombolytics be initiated within 12 hours of the onset of symptoms and preferably within six hours. Additionally, the diagnosis of STEMI and administration of thrombolytics should occur within 30 minutes of arriving at the hospital. The major risk associated with the use of thrombolytics is stroke (intracerebral hemorrhage). Therefore, patients must be carefully selected before receiving thrombolytics and the diagnosis of STEMI confirmed prior to use. The use of alteplase (t-PA) is also recommended for the treatment of acute ischemic strokes but only if used within three to four-and-a-half hours of symptom onset.

A 70-year-old African-American man is hospitalized for ischemic stroke. His medical history is significant for hypertension and dyslipidemia × 20 years. He currently smokes half of a pack of cigarettes/day and drinks one to two drinks/night.

Allergies: NKDA

Medications: Atenolol 50 mg/chlorthalidone 25 mg tablet 1 po daily; atorvastatin 80 mg tablet 1 po daily; aspirin 81 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 220 lb Ht 71 in T 98.6°F BP 135/78 HR 70 RR 18 BMI 30.7

SCr 1.1 TC 190 LDL 108 HDL 45 TG 185

The patient is treated with anticoagulation and supportive care and sent to a stroke rehabilitation unit four days later.

What type of antiplatelet therapy would be best to begin for secondary stroke prevention in this patient?

Dipyridamole	Antiplatelet agent (dipyridamole, aspirin, clopidogrel, prasugrel, ticlopidine)
Mechanism of Action	Inhibition of platelet aggregation and thrombus formation; vasodilation (dipyridamole)
***Contraindications*/ Precautions**	*Hypersensitivity, bleeding disorders, children, hematopoietic disorders*/Risk of bleeding, thrombotic thrombocytopenic purpura, hepatic impairment, renal impairment, concurrent use of CYP2C19 inhibitors, poor metabolizers of CYP2C19, gastrointestinal disease, heavy ethanol use, concurrent NSAID/COX-2 inhibitor use, patients ≥75 years of age
Adverse Effects	Bleeding, nausea, vomiting, dyspepsia, gastrointestinal ulcers/erosions, anemia, rash, neutropenia (ticlopidine), dizziness, headache, anaphylaxis, and cardiac disorders with use of IV injection (dipyridamole)
Drug Interactions	NSAIDs, CPY2C19 substrate (clopidogrel), methotrexate, anticoagulants. Multiple interactions exist—consult prescribing information.
Monitoring	Signs/symptoms of bleeding or thrombosis, hemoglobin, hematocrit, CBC (ticlopidine), ECG (dipyridamole)
Case Notes	Dual antiplatelet therapy with aspirin (25 mg) and dipyridamole (200 mg) is recommended for secondary prevention of stroke. This combination is preferred over either agent alone. In studies, a sustained-release form of the combination was used and is the preferred form to use. Clopidogrel or aspirin may also be used for secondary prevention of stroke. In those patients that fail single agents for primary prevention, the combination therapy would be an appropriate option, like in this patient. Combination clopidogrel and aspirin is not recommended due to an increased risk of bleeding. Prasugrel is not recommended for use in stroke prevention at this time due to increased risk of bleeding. Warfarin therapy is effective for stroke prevention in patients with atrial fibrillation, but it is not more effective than aspirin alone for secondary prevention of stroke from other causes and has a higher risk of bleeding.

A 19-year-old woman presents to her primary care provider with concerns about her acne. She has a history of facial acne since age 15. Initially, benzoyl peroxide plus erythromycin gel was beneficial, but it caused excessive drying. Adapalene was used next and it controlled her acne for about six months, but the acne worsened and oral antibiotics were added. Most recently, she has completed two, three-month courses of minocycline over the past six months that have failed to control her acne outbreaks. She has also noted some scarring from her acne and cyst formation the past few months.

Allergies: NKDA

Medications: Adapalene topical gel applied daily after washing face; combined oral contraceptive tablet 1 po daily

Physical Exam/Other Studies:

Wt 125 lb Ht 64 in T 98.5°F BP 110/70 HR 77 RR 16

Physical exam reveals multiple acne lesions on her face and chest areas. Some cystic lesions and scarring are also present.

SCr 1.0 Fasting glucose 80

Which of the following medications would be the best option to improve her acne and reduce the number of acne lesions?

A. doxycycline
B. azelaic acid
C. isotretinoin
D. benzoyl peroxide

Isotretinoin	Oral retinoid (no other agents in the class)
Mechanism of Action	Reduces sebaceous gland size and sebum production, inhibits *P acnes* growth, alters keratinization, inhibits inflammation
***Contraindications*/ Precautions**	*Hypersensitivity to retinoids or vitamin A, pregnancy*/Hyperlipidemia, diabetes, severe osteoporosis, hearing impairment, dermatologic disorders, growth effects, skin cancers, hepatitis, elevated liver enzymes, inflammatory bowel disease, papilledema, history of psychiatric disorders
Adverse Effects	Dryness of the nasal, mouth and eye mucosa, cheilitis, skin desquamation, hypercholesterolemia, hypertriglyceridemia, photosensitivity, liver function changes with hepatomegaly, arthralgias, muscle stiffness, headaches, dermatologic disorders. Multiple adverse reactions exist—consult prescribing information for complete list.
Drug Interactions	Avoid concomitant use of vitamin A and tetracyclines. Levels of isotretinoin may be increased by alcohol and tetracyclines. Isotretinoin may decrease levels of contraceptives.
Monitoring	Pregnancy tests, lipid profiles, liver function tests, CBC with differential, platelets, sedimentation rate, glucose, CPK, mood changes, skin reactions
Case Notes	Isotretinoin is the most effective agent for the treatment of inflammatory acne. It would be an appropriate choice in patients with acne who experience scarring or those who have failed to achieve clearing of acne with other treatments. Oral or topical antibacterials and topical retinoids are not as effective as isotretinoin at resulting in remission of acne lesions. Isotretinoin is a well documented teratogen. It is category X in pregnancy. All patients must participate in the iPLEDGE program, which requires regular pregnancy testing. Dosing of isotretinoin ranges from 0.5-1mg/kg/day. Optimal results generally occur when a cumulative dose of 120-150 mg/kg is achieved. Most patients will achieve a 50% reduction in lesions after 2-4 weeks of treatment.

A 14-year-old boy is seen at his dermatologist's office for acne. One month ago, he was started on tazarotene. His acne was cleared by the medication, however he has experienced skin dryness. He would like to try another agent.

Allergies: Tetracyclines (rash, hives, facial swelling)

Medications: Tazarotene 0.1% gel applied to affected areas daily

Physical Exam/Other Studies:

Wt 155 lb Ht 70 in T 98.5°F BP 110/70 HR 75 RR 18

Physical exam reveals multiple acne lesions on face and chest and back.

Which of the following agents would be appropriate to start at this point?

A. tretinoin
B. oral minocycline
C. isotretinoin
D. topical erythromycin

Topical erythromycin	Topical antibacterials (erythromycin, clindamycin, azelaic acid)
Mechanism of Action	Comedolytic with activity against *P acnes*
***Contraindications/* Precautions**	*Hypersensitivity, previous pseudomembranous colitis (clindamycin)*/Skin irritation, hypopigmentation (azelaic acid)
Adverse Effects	Skin dryness, erythema, scaling, pruritus, skin irritation, hypopigmentation (azelaic acid), diarrhea and pseudomembranous colitis (clindamycin). Adverse effects vary with individual agents—consult prescribing information.
Drug Interactions	Avoid concomitant use with BCG (erythromycin, clindamycin)
Monitoring	Response to therapy
Case Notes	Topical erythromycin would be an appropriate agent to try in this patient before moving to oral therapies. The addition of another topical retinoid would only increase adverse effects without significantly improving acne. Oral isotretinoin could be used if the patient's acne worsens or if he fails other therapies, but would not be appropriate in this patient with mild to moderate acne as initial therapy. Oral antibacterials would be another appropriate treatment option. However since this patient is allergic to tetracyclines, oral minocycline would not be an appropriate agent to use. Topical antibacterials should be applied to the affected areas twice daily. Benzoyl peroxide, another topical agent for the treatment of acne, may also have antibacterial activity in addition to comedolytic activity. Using erythromycin in combination with benzoyl peroxide increases efficacy at reducing acne lesions and decreases the likelihood of bacterial resistance to the topical erythromycin.

A 14-year-old boy is seen at his dermatologist's office with complaints of acne. He has been experiencing multiple breakouts of acne lesions on his face, chest and back. He has been trying over-the-counter medications containing salicylic acid, but they are not working very well to clear the lesions. He has no medical conditions.

Allergies: NKDA

Medications: Salicylic acid 2% acne wash (OTC) twice daily

Physical Exam/Other Studies:

Wt 155 lb Ht 70 in T 98.5°F BP 110/70 HR 75 RR 18

Physical exam reveals multiple acne lesions on face and chest and back.

Which of the following agents would be appropriate to start at this point?

A. isotretinoin
B. oral minocycline
C. corticosteroids
D. tazarotene

Tazarotene	Topical retinoid (tretinoin, adapalene, tazarotene)
Mechanism of Action	Comedolytic agent that increases cell turnover in the follicle and decreases cellular adhesion
***Contraindications*/ Precautions**	*Hypersensitivity to retinoids or vitamin A, pregnancy(tazarotene)*/Photosensitivity, skin irritation, eczema
Adverse Effects	Skin dryness, erythema, scaling, pruritus, skin irritation, hyper or hypopigmentation, photosensitivity, edema, stinging, blistering, initial acne flare-up
Drug Interactions	Topical retinoids may decrease the efficacy of oral contraceptives. Vitamin A may increase the toxicities of topical retinoids.
Monitoring	Acne severity, skin reactions, pregnancy tests (tazarotene)
Case Notes	Topical retinoids would be an appropriate therapeutic option for this patient. They are effective for the treatment of mild to moderate acne. Oral therapies would not be appropriate at this point since the patient has not failed topical treatments and has mild to moderate acne. Topical and oral corticosteroids might be appropriate in patients who have severe forms of acne, but are not indicated in this patient. Of the retinoids, tazarotene is the most effective topical retinoid. However, skin irritation may limit the use of tazarotene. Adapalene may produce less skin irritation and discoloration than tazarotene and tretinoin. Topical retinoids should be applied once daily usually at bedtime. Start with the lowest concentration every other day or daily and increase as tolerated to limit adverse effects. Patients should also be advised to wear sunscreen daily while using topical retinoids.

An 8-year-old girl is seen at her pediatrician's office for a routine visit. She has a history of allergic rhinitis, food allergies and atopic dermatitis. As-needed topical corticosteroids control her symptoms normally but she has experienced some exacerbations recently that are not completely controlled with steroids. Her mother has brought her to the clinic today to see if there is anything else to help with the symptoms. She is concerned about using topical corticosteroids for such long periods of time.

Allergies: NKDA

Medications: Cetirizine 10 mg tab (OTC) 1 po daily at bedtime; mometasone nasal spray 1 spray in each nostril daily; triamcinolone acetonide lotion 0.1% applied to affected areas daily

Physical Exam/Other Studies:

Wt 65 lb Ht 51.6 in T 98.5°F BP 110/70 HR 86 RR 18

Physical exam reveals multiple areas of eczematous skin lesions on the torso, extremities and face. Several of the lesions are excoriated and appear inflamed.

What would be an appropriate topical therapy to begin that may improve the patient's symptoms?

Topical immunomodulators	Tacrolimus, pimecrolimus
Mechanism of Action	Inhibition of calcineurin which decreases T-cell activation and cytokine production resulting in decreased inflammation
***Contraindications*/ Precautions**	*Hypersensitivity*/Malignancy, local reactions, lymphadenopathy, skin papilloma, infection
Adverse Effects	Headache, fever, burning, pruritus, erythema, flu-like symptoms, nasopharyngitis, cough
Drug Interactions	Avoid the use of topical immunomodulators with immunosuppressants. The effects may be increased by antidepressants, azole antifungal agents, calcium channel blockers, 3A4 inhibitors.
Monitoring	Response to therapy
Case Notes	Topical immunomodulators are a good option for patients with atopic dermatitis in whom the use of corticosteroids is a concern. They may also benefit patients whose symptoms are not controlled with corticosteroids alone or who are not responding to other therapies. The FDA issued a boxed warning regarding the risk of skin cancer and lymphomas with the use of topical immunomodulators. The FDA recommends that these agents should be used intermittently or for short term use only on affected areas as needed to control symptoms. Patients should be advised of this risk when dispensing these products prior to their use. Dosing for use in atopic dermatitis is as follows: tacrolimus 0.1% ointment twice daily (adults); tacrolimus 0.03% ointment twice daily (children older than 2 years of age); pimecrolimus 1% cream twice daily (children and adults)

A 4-year-old boy is seen at his pediatrician's office for a routine visit. He has a medical history that includes asthma and allergic rhinitis. His mother has noticed that he has a rash that he cannot stop scratching on his face and extremities.

Allergies: NKDA

Medications: Pulmicort 0.5 mg respule 1 inhaled via nebulizer twice daily; albuterol MDI 1–2 puffs every 4 hours as needed for asthma exacerbations; loratadine 5 mg/5 ml syrup (OTC) 1 teaspoonful po once daily

Physical Exam/Other Studies:

Wt 30 lb Ht 40 in T 98.5°F BP 98/56 HR 96 RR 18

Physical exam reveals multiple areas of eczematous skin lesions on the torso and extremities. Some of the lesions appear inflamed and excoriated.

His physician diagnoses him with atopic dermatitis.

What would be an appropriate topical therapy to begin?

Topical corticosteroids	Betamethasone dipropionate, clobetasol propionate, halobetasol propionate, fluocinonide, triamcinolone acetonide, fluticasone propionate, betamethasone valerate, hydrocortisone valerate, mometasone furoate, desonide, hydrocortisone butyrate, hydrocortisone
Mechanism of Action	Anti-inflammatory
***Contraindications*/ Precautions**	*Hypersensitivity, fungal infections*/adrenal suppression, immunosuppression, skin reactions, Kaposi's sarcoma
Adverse Effects	Local skin atrophy, striae, telangiectasia, acneiform eruptions, adrenal suppression, contact dermatitis, rebound flare of symptoms with discontinuation
Monitoring	Response to therapy, signs of infection
Case Notes	Topical corticosteroids are the standard agents used in the treatment of atopic dermatitis. They are effective at controlling inflammation and pruritus. Most commonly, high potency agents are used once or twice daily for short periods of time to control symptoms then decreased to the lowest potency that will control the symptoms. High potency agents should not be used on areas of thin skin (eg, eyelids, face, groin, axilla). If topical steroids are needed on the face, a lower potency agent should be used. Also lower potency agents should be selected for use in children. The vehicle is important as well. Ointments are more occlusive and stronger than creams. Ointments may not be preferable to use on hair-covered areas. Gels may be more appropriate to use on hair-covered areas.

A 14-year-old girl is seen by her pediatrician for a burn. She has a second-degree or superficial partial-thickness burn on her arm that occurred earlier today. Her past medical history is noncontributory. Her pain is a 5/10 right now.

Allergies: Sulfonamides (anaphylaxis)

Medications: Acetaminophen 500 mg tablet (OTC) 1 po every 6 hours for pain (no more than 5 doses/day)

Physical Exam/Other Studies:

Wt 108 lb Ht 54 in T 98.5°F BP 110/70 HR 70 RR 16

Physical exam reveals a superficial to deep partial-thickness burn on her arm covering approximately 2% of her total body surface area.

Which topical antimicrobial therapy should be avoided in this patient?

A. silver sulfadiazine
B. mafenide
C. mupirocin
D. bacitracin/polymixin/neomycin

Silver sulfadiazine	Topical Antimicrobial (silver sulfadiazine, silver nitrate, mafenide, bacitracin/polymixin/neomycin, chlorhexidine, mupirocin, povidone iodine)
Mechanism of Action	Bactericidal or bacteriostatic against bacteria, fungi and some viruses
***Contraindications*/ Precautions**	*Hypersensitivity, premature infants or < 2 year old*/Risk of superinfection with prolonged use, hepatic or renal impairment
Adverse Effects	Local skin reactions, allergic reactions, skin discoloration, fungal overgrowth
Drug Interactions	Avoid use with BCG
Monitoring	Signs/symptoms of infection, patients with long-term use or extensive burns monitor: serum electrolytes, renal function tests, CBC, urinalysis
Case Notes	Topical antimicrobial agents are appropriate to use for infection prevention in full-thickness or deep partial-thickness burns. The choice of agent is determined by patient factors and the antimicrobial coverage provided by the drug. Silver sulfadiazine has classically been used as the preferred topical antimicrobial in the treatment of burns. However, this drug should not be used in patients with sulfonamide allergies. Ambulatory burn management also includes pain control with analgesic agents and cleansing and wound dressings for the burn. Moderate to severe burns should be treated inpatient in the hospital. In addition to analgesics and wound dressings, these types of burns should be treated with fluid resuscitation to prevent shock and multiorgan failure with IV fluids, oxygen for pulmonary edema and inhalation injury, parenteral nutrition and IV, oral and topical antimicrobials to prevent infection. Inpatient treatment of burns also includes cleansing of the burn area with debridement and skin grafting. Both inpatient and ambulatory treatment of burns should include tetanus vaccination.

A 55-year-old woman with a 30+ year history of plaque type psoriasis presented to the outpatient dermatology clinic two days ago with another flare-up of her psoriasis. She was diagnosed at age 23 and initially responded to topical therapy with coal tar products and corticosteroids. She subsequently required photochemotherapy using psoralens with UVA phototherapy. Five years ago, she started on oral methotrexate. This had kept her condition under control until recently. Now she is having worsening and more frequent exacerbations of her psoriasis.

Allergies: Topical psoralens (rash, severe skin reactions)

Medications: Methotrexate 5 mg tablet 1 po three times per week; lisinopril 10 mg tablet 1 po every morning

Physical Exam/Other Studies:

Wt 140 lb Ht 63 in T 99.0°F BP 128/88 HR 80 RR 20

Physical exam reveals multiple plaques on arms, legs, back and scalp

Which of the following pharmacotherapies would be the best therapeutic option for this patient to reduce her psoriasis symptoms?

A. cyclosporine
B. topical coal tar
C. methoxsalen
D. infliximab

Infliximab	Biologic Agents (infliximab, etanercept, adalimumab, alefacept)
Mechanism of Action	Inhibition of the tumor necrosis factor alpha (infliximab, etanercept, adalimumab); Prevent activation of T-cells (alefacept)
***Contraindications*/ Precautions**	*Hypersensitivity, serious infection*/Infections, tuberculosis, autoimmune disorders, CNS demyelinating disorders, hepatitis, heart failure, hematologic disorders, hepatic injury, immune suppression, infusion reactions. Contraindications/precautions listed are general for all agents. Warnings vary with individual agents. Please consult prescribing information for comprehensive list.
Adverse Effects	Infusion/injection site pain and inflammation, headache. Adverse reactions vary with individual agents. Please consult prescribing information for a comprehensive list.
Drug Interactions	BCG, tacrolimus, live virus vaccines. Please consult prescribing agent for comprehensive list for each agent.
Monitoring	Tb testing, signs of infection, CBC
Case Notes	Because this patient has failed topical and oral immunosuppressants, biologic agents would be an appropriate option to control psoriasis symptoms. These agents are efficacious at inducing remission of psoriasis symptoms; however the high cost and serious adverse effects associated with these therapies necessitate that they should be reserved for patients not responding to other therapies or for patients with severe psoriasis. Doses of the agents in this class: infliximab 5 mg/kg IV infusion; etanercept 50 mg subcutaneous injection; adalimumab 80 mg subcutaneous injection followed by 40 mg subcutaneous injection; alefacept 15 mg intramuscular injection. These agents are usually administered at weekly or monthly intervals. Tuberculosis infections have been associated with the use of biologic agents. Tb skin testing is recommended prior to therapy and during therapy to monitor for the occurrence of these infections.

A 30-year-old woman with a year history of plaque type psoriasis presents to her dermatology clinic with a flare up of her psoriasis. She had responded to topical treatments initially but these have failed to control her symptoms for the last several months. She tried oral psoralens + UVA in the past but could not tolerate the adverse effects. She does not have any other medical conditions.

Allergies: NKDA

Medications: Combined oral contraceptive tablet 1 by mouth daily

Physical Exam/Other Studies:

Wt 130 lb Ht 65 in T 98.5°F BP 128/78 HR 77 RR 18

Physical exam reveals multiple plaques on arms, legs, back and scalp

Which of the following pharmacotherapies would be the best therapeutic option for this patient?

A. cyclosporine
B. topical coal tar
C. methoxsalen + UVA
D. infliximab

Cyclosporine	Calcineurin inhibitor (cyclosporine, tacrolimus)
Mechanism of Action	Inhibition of T-cell activation
***Contraindications*/ Precautions**	*Hypersensitivity, abnormal renal function, uncontrolled hypertension, malignancies, concomitant UVA/UVB therapy, immunosuppressant or coal tar use*/Skin cancers, hepatotoxicity, infection, hypertension
Adverse Effects	Hypertension, edema, headache, increased triglycerides, nausea, diarrhea, gum hyperplasia, hirsutism, tremor, paresthesias, renal dysfunction/nephropathy, infection, dizziness, vomiting, flatulence, insomnia
Drug Interactions	Immunosuppressive agents, live virus vaccines, CYP3A4 inhibitors may increase cyclosporine levels, cyclosporine may increase levels of CYP3A4 substrates.
Monitoring	Blood pressure, CBC, renal function tests, lipid profiles, serum electrolytes, uric acid, glucose
Case Notes	Cyclosporine would be an acceptable treatment for this patient since she is no longer responding to topical therapies alone, such as coal tar, and is not a candidate for UV therapy with methoxsalen and UVA due to prior intolerance. Immunosuppressants such as cyclosporine, methotrexate, tacrolimus, pimecrolimus have all been used in the treatment of moderate to severe psoriasis with benefit. These agents may cause serious adverse effects so the risk versus benefit must be considered before therapy is initiated. Biologic agents would also be an option, however it would be appropriate to assess the patient's response to therapy with oral immunosuppressants before moving to biologic agents due to the high cost and adverse effect profile of these agents. Doses of the agents in this class: cyclosporine (2.5-5 mg/kg po daily); tacrolimus (0.05 mg/kg/day-0.15 mg/kg/day). Tacrolimus has not been approved for use in the treatment of psoriasis although it has been used for patients not responding to other approved therapies.

A 15-year-old is seen at a dermatologist's office for treatment of his psoriasis. He has tried emollients and topical steroids, which are helping, but he still has some lesions that are not controlled completely. He tried tazarotene gel, but it caused a lot of skin irritation and dryness, so he would like to try something else. He has no medical conditions.

Allergies: NKDA

Medications: Loratadine 10 mg tablet (OTC) 1 po daily; betamethasone 0.1% cream applied to affected areas twice daily

Physical Exam/Other Studies:

Wt 154 lb Ht 59 in T 97.8°F BP 118/77 HR RR 20

Physical exam reveals a few psoriasis lesions on legs and elbows

Which topical therapy would be an appropriate next step for the treatment of this patient's psoriasis?

Calcipotriene	Topical vitamin D analog
Mechanism of Action	Inhibits keratinocyte proliferation and differentiation
***Contraindications*/ Precautions**	*Hypersensitivity, vitamin D toxicity*/Skin irritation
Adverse Effects	Burning, stinging, pruritus, rash, erythema, dermatitis, dry skin
Drug Interactions	None with topical therapy
Monitoring	Serum calcium levels
Case Notes	A topical vitamin D analog is an appropriate topical agent to try in this patient who is achieving partial remission in his symptoms with topical steroids and emollients. Most patients will respond to calcipotriene within two weeks. The use of this product is limited by its potential to cause hypercalcemia, thus no more than 100 g/week should be used. Calcipotriene is applied topically to lesions one to two times daily. Although an oral vitamin D analog product is available it is not indicated for use in the treatment of psoriasis in the U.S.

A 69-year-old man presents to the pharmacy after a visit to his optometrist. He tells you that he was diagnosed with open-angle glaucoma and wants to know more about this eye drop his doctor prescribed him before he fills it. He can't remember the name of it but tells you his doctor says it's available in a generic and is one of the most commonly prescribed agents for his type of glaucoma. He says it is first-line treatment and before prescribing it, the doctor checked his pulse and asked him a lot of questions about his heart function and breathing disorder history, of which he has no problems. He has a past medical history of BPH, HTN, dyslipidemia, and macular degeneration.

Allergies: NKDA

Medications: Valsartan 160 mg tablet 1 po daily; doxazosin 2 mg tablet 1 po twice daily; atorvastatin 40 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 187 lb Ht 69 in BP 138/89 HR 88
Physical exam not performed.

What open-angle glaucoma medication class was this patient prescribed?

Beta-adrenergic Blocking Agent	Betaxolol, carteolol, levobunolol, metipranolol, timolol
Mechanism of Action	Decreases the production of aqueous humor and possibly outflow by blocking the $beta_1$- and $beta_2$-adrenergic receptors in the ciliary body, thus reducing intraocular pressure
***Contraindications/* Precautions**	*Hypersensitivity to any component of the formulation, sinus bradycardia, sinus node dysfunction, heart block greater than 1st degree, cardiogenic shock, uncompensated heart failure, pregnancy (2nd and 3rd trimesters) /* Abrupt withdrawal, anaphylactic reactions, bronchospastic disease, conduction abnormalities, diabetes, heart failure, myasthenia gravis, PVD, pheochromocytoma, psoriasis, psychiatric disease, renal impairment, contact lens wearers
Adverse Effects	Ocular burning, stinging, headache, blepharitis, blurred vision, cataract, conjunctivitis, foreign body sensation, itching, tearing, infection, and rarely bradycardia and/or hypotension
Drug Interactions	Major substrate of CYP2D6; avoid use with methacholine; use caution with alpha-/beta-agonists, $alpha_1$-blockers, antihypertensives, theophylline; see monograph for complete listing
Monitoring	BP, pulse, ocular infections, response to therapy
Case Notes	Based on the questions the physician asked this patient before prescribing an agent for open-angle glaucoma, he was most likely prescribed a beta-blocker such as timolol. Instruct patients to remove contact lenses before instilling drops and wait 15 minutes before reinserting. Alternative first-line treatments for open-angle glaucoma are prostaglandins, like latanoprost, bimatoprost, travoprost, or brimonidine, all of which are appropriate in the event of a contraindication to beta-blocker therapy. Combination products with timolol plus dorzolamide, a carbonic anhydrase inhibitor, or timolol plus brimonidine, an $alpha_2$-adrenergic agonist are available as well. These products would be good options in a patient with refractory elevated intraocular pressure not controlled by a single agent.

A 48-year-old woman returns to the clinic for a routine follow-up visit about her diabetes. She has a past medical history of Type 2 diabetes, hypertension, and dyslipidemia. She was diagnosed with new-onset Type 2 diabetes about two years ago and her elevated glucose levels have been treated solely with insulin since then. Upon diagnosis, she also received formal education about diabetes from the clinic's clinical pharmacist and dietitian, both of whom are certified diabetes educators. The education sessions enlightened and motivated the patient to adopt new and healthy lifestyle changes. She significantly reduced the amount of carbohydrates in her meals to recommended quantities and implemented a consistent daily exercise routine. Her glucose levels and A1c have been at goal for several months and her PCP has been reducing her insulin doses to avoid hypoglycemia.

Today, she presents hoping to stop her insulin and switch to oral medications to maintain control of her diabetes. The PCP feels this is possible due to her new and appropriate lifestyle habits and current level of control.

Allergies: NKDA

Medications: Insulin glargine 16 units every evening; insulin aspart four units with breakfast, four units with lunch, and six units with dinner; lisinopril 10 mg tablet 1 po daily; simvastatin 20 mg tablet po every evening

Physical Exam/Other Studies:

Wt 160 lb Ht 70 in T 98.6°F BP 116/76 HR 72 RR 12 O_2 sat 99%

Physical exam reveals no pertinent findings.

A1c 6.3% fasting glucose 97 LDL 84 TG 144 HDL 55 SCr 1.0 K 3.9

As the clinical pharmacist and certified diabetes educator in this facility, the PCP asks what oral diabetes medication would be most appropriate as a first step to replace this patient's insulin regimen. What do you recommend?

Biguanide	Metformin
Mechanism of Action	Reduces glucose production in the liver, improves insulin sensitivity, and reduces absorption of glucose in the gastrointestinal tract
***Contraindications/* Precautions**	*Hypersensitivity to metformin; renal dysfunction (specifically a SCr ≥1.5 mg/dL in males or ≥1.4 mg/dL in females or Crcl <60)/* CHF requiring pharmacologic management, liver dysfunction, or renal dysfunction can increase risk of lactic acidosis. Do not start metformin in patients ≥80 years old until normal renal function is confirmed. Safety and efficacy have not been established in children <10 years of age. Temporarily discontinue therapy prior to administration of iodinated contrast media due to potential for acute alteration of renal function and hold for at least 48 hours.
Adverse Effects	Diarrhea, nausea, vomiting; rarely: lactic acidosis, hypoglycemia, decreased vitamin B12 levels
Drug Interactions	None significant; limit ethanol due to increased risk of lactic acidosis
Monitoring	Blood glucose, A1c, initial and periodic renal function, vitamin B12 and folate if anemic
Case Notes	Metformin is the preferred initial oral diabetes agent according to the 2010 ADA Standards of Care. Metformin is one of the most effective oral monotherapy agents and may lower the A1c one to two percent. Metformin is preferred in this patient because it may cause weight loss, which is desirable because of the prevalence of obesity in Type 2 diabetes, and because other common initial agents may cause weight gain. At diagnosis, a patient may require initial insulin therapy to gain control of elevated glucose levels, especially with an A1c >11 percent. Once controlled to a goal of <7 percent (per ADA) or <6.5 percent (per AACE) and adoption of appropriate diet and exercise habits, it may be possible to switch from insulin therapy to oral therapy. To avoid the common adverse effect of diarrhea, metformin must be initiated at low doses and taken with food (ideally mid-meal); titrate doses weekly; diarrhea may resolve with time. Metformin dose: 500-2,550 mg in divided doses.

A 52-year-old man presents to his PCP's office for a routine follow-up visit on diabetes. His past medical history is significant for Type 2 diabetes, heart failure, hypertension, and dyslipidemia. His diabetes was diagnosed one year ago and he has only been prescribed metformin for treatment. His metformin dose was optimized last month, but his blood glucose levels are still not at goal. However, he did notice an improvement with the dose increase and with recent diet and exercise improvements. His heart failure has not been very stable lately and his PCP has been adjusting his diuretic dose to reduce pedal edema.

Allergies: Penicillin (rash)

Medications: Metformin 850 mg tablet 1 po three times daily with meals; lisinopril 40 mg tablet 1 po daily; metoprolol succinate 100 mg tablet 1 po daily; furosemide 40 mg tablet 1 po twice daily; atorvastatin 40 mg tablet 1 po every evening; aspirin 81 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 220 lb Ht 72 in T 98.4°F BP 112/66 HR 62 RR 15 O_2 sat 99%

Physical exam reveals 2 + pitting edema bilaterally at lower legs.

A1c 8.5% fasting glucose 213 LDL 66 TG 256 HDL 39 SCr 1.1 K 4.3

The PCP adjusts the furosemide to address the pedal edema and calls you, the clinic pharmacist, for advice on starting a new medication to treat the patient's diabetes. The patient refuses to start insulin at this time.

You need to add an oral agent that is safe, given the patient's PMH, and effective enough to potentially attain a goal A1c of <7 percent. What drug class do you recommend?

Sulfonylurea	Glipizide, glyburide, glimepiride
Mechanism of Action	Stimulates insulin release from the pancreatic beta cells
***Contraindications/* Precautions**	*Hypersensitivity to the medication; previously severe sulfonamide allergy; diabetic ketoacidosis; Type 1 diabetes*/Renal impairment (glyburide is not recommended if Clcr <50; glipizide is not recommended if Clcr <10); risk of hypoglycemia.
Adverse Effects	Hypoglycemia, weight gain, others uncommon
Drug Interactions	Beta blockers may mask signs and symptoms (except sweating) and enhance/prolong hypoglycemia; may enhance effects of other hypoglycemic agents; glipizide and glimepiride are CYP2C9 substrates
Monitoring	Blood glucose, A1c, signs/symptoms of hypoglycemia
Case Notes	Sulfonylureas and metformin may each lower the A1c by one to two percent. Therefore, a sulfonylurea may have the potential to attain the goal A1c in this patient. TZDs may lower A1c nearly as much as sulfonylureas or metformin, but a TZD is not appropriate in this case due to the recent history of edema with heart failure. Other oral agents are not as potent in regard to A1c lowering and may not be as effective at this time. Counsel patients to take sulfonylureas in relation to a meal (with food); glipizide is optimally taken 30 minutes prior to meals, once or twice daily; glipizide XL may be taken once daily with a meal; glyburide may be taken once or twice daily with meals; glimepiride is taken once daily with the first main meal. If a dose is to be taken, but that corresponding meal is skipped, then the dose should not be taken to avoid risk of hypoglycemia. Hypoglycemia is often due to an extended time without eating. Glipizide dosing: 2.5-40 mg daily in two divided doses (maximum dose of glipizide XL is 20 mg). Glyburide dosing: 2.5-20 mg daily in two divided doses. Glimeperide dosing: 1-8 mg once daily.

A 44-year-old woman returns to your pharmacotherapy service for diabetes management. Her past medical history includes Type 2 diabetes (diagnosed about six years ago), hypertension, dyslipidemia, and obesity. She has been a patient in your outpatient service for nine months now and her glucose control has been improving. She has been working to adjust her diet and become consistent with an exercise routine, but further improvements are still needed. She is taking three oral medications for her diabetes and checks her blood glucose twice daily alternating between breakfast and dinner one day, and then lunch and bedtime the next day; all fingersticks are done before meals or at bedtime. Her glucose readings have improved over the past several months after various medication titrations and these pre-meal values are mostly at goal of 70-130 mg/dL. These values have been consistently within goal range for the past three months.

Allergies: NKDA

Medications: Metformin 1,000 mg tablet 1 po twice daily; glipizide 10 mg tablet two po twice daily; pioglitazone 45 mg tablet 1 po once daily; lisinopril 20 mg tablet 1 po once daily; hydrochlorothiazide 12.5 mg tablet 1 po daily; pravastatin 40 mg tablet 1 po every evening; aspirin 81 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 254 lb Ht 75 in T 98.6°F BP 122/78 HR 82 RR 12 O_2 sat 98%

Physical exam reveals an obese female in no acute distress.

A1c 7.9% LDL 104 TG 184 HDL 42 SCr 1.1 K 4.0

You assess that while her fingerstick glucose values have been within goal range for three months, her A1c is still not improving to goal. You have her assess blood glucose levels two hours after eating and discover elevations well above the goal of <180 mg/dL. You decide that her glipizide is not adequately addressing her post prandial needs.

If you stop her glipizide, with what oral agent can you replace it to address post prandial elevations?

Meglitinide (may also be called glinides, or non-sulfonylurea secretagogues)	Repaglinide, nateglinide
Mechanism of Action	Stimulates insulin release from pancreatic beta cells; binding sites are adjacent to sulfonylurea binding sites; nateglinide causes insulin release that is dependent on existing glucose levels
***Contraindications*/ Precautions**	*Hypersensitivity to the drug agent, diabetic ketoacidosis, type 1 diabetes, concurrent gemfibrozil therapy (for repaglinide only)*/ May cause hypoglycemia—use caution in patients more susceptible to glucose-lowering effects such as those with hepatic, renal, or adrenal/pituitary impairment, elderly, or malnourished
Adverse Effects	Hypoglycemia, weight gain
Drug Interactions	Gemfibrozil and azole anti-fungals may increase repaglinide serum concentration, ethanol (may increase hypoglycemia risk)
Monitoring	Glucose levels, A1c
Case Notes	Meglitinides are short-acting secretagogues and, therefore, may be more effective for post-prandial glucose elevations than for pre-prandial elevations. They should not be used concomitantly with sulfonylureas, so this patient's glipizide should be stopped. Meglitinides may be expected to lower the A1c 0.8-1 percent, so they may be appropriate for patients nearing the A1c goal, especially with post-prandial glucose elevations. Meglitinides should be dosed at 15-30 minutes before each meal and skipped if the meal will not be eaten. Repaglinide dosing: 0.5-4 mg taken with meals to a maximum of 16 mg daily in divided doses. Nateglinide dosing: 60-120 mg taken with meals three times daily

You are a pharmacist practicing in a community pharmacy chain store. A 34-year-old male patient that you know well, and have helped many times before, presents for a refill of his routine medications. He has a past medical history of Type 2 diabetes and hypertension. You have taught him to use his glucometer at previous visits and regularly check his blood pressure. Last month, he was started on basal insulin along with his oral medications and you instructed him on proper insulin-injection technique. Today, you notice as he approaches the counter, that his shoes are untied and loose. You ask him about his untied shoes. The patient replies that he is wearing his shoes that way on purpose, due to profound swelling he has been experiencing in his feet and lower legs for the past two weeks. He denies SOB, CP, or dizziness.

Allergies: NKDA

Medications: Metformin 850 mg tablet 1 po three times daily; glyburide 5 mg tablet two po twice daily; pioglitazone 45 mg tablet 1 po once daily; insulin glargine inject 20 units subcutaneously every evening; lisinopril 10 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 220 lb Ht 80 in BP 112/68 HR 84 RR 12

Physical exam reveals a male in no acute distress with 2+ pitting edema bilaterally.

Pertinent lab values obtained from calling the physician office include:

A1c 8.1% SCr 0.9 K 4.2

The patient reports compliance with all medications including his new insulin. After assessing the patient and his recent history, you decide to call the PCP to recommend stopping one of his diabetes medications due to the lower extremity edema.

Which diabetes medication is most likely responsible for his new edema?

Thiazolidinedione (TZD)	Pioglitazone and rosiglitazone
Mechanism of Action	TZDs are agonists for peroxisome proliferator-activated receptor-gamma (PPAR gamma); stimulation of PPAR gamma leads to increased insulin sensitivity in muscle and adipose tissue
Contraindications/ Precautions	*NYHA class III-IV heart failure*/TZD may cause edema, so use caution in those already with edema; NYHA class I-II heart failure; may be associated with increased risk of angina or MI (conflicting studies can neither confirm nor refute an association with rosiglitazone); bone fracture risk (in patients with post-menopausal osteoporosis); hepatic impairment; use with insulin increases risk of edema
Adverse Effects	Hypoglycemia, weight gain, LDL and HDL may increase with rosiglitazone, HDL may increase and TG may decrease with pioglitazone, edema, fractures; rarely: hepatic injury
Drug Interactions	Insulin may increase risk of edema
Monitoring	Glucose levels, A1c, LFT at baseline and periodically, signs of edema
Case Notes	One of the main adverse effects of TZDs is peripheral edema (this results from increased sodium reabsorption as an effect of stimulating PPAR gamma systems). That alone may have prompted you to stop the pioglitazone. However, this patient had been stable on his pioglitazone without edema until two weeks ago. He started an insulin regimen four weeks ago. Insulin use can increase the risk of edema caused by TZDs. This patient's glucose was not controlled on triple oral therapy, so the insulin is appropriate and needed. The TZD must be stopped because the edema could lead to the development of heart failure. Pioglitazone dosing: 15-45 mg once daily Rosiglitazone dosing: 2-8 mg daily (may be given once daily or divided twice daily; most effective if divided twice daily). TZDs may lower the A1c by 0.5-1.5 percent.

A 53-year-old man returns to his doctor's office for a diabetes visit. He has a past medical history pertinent for Type 2 diabetes (12 years), hypertension, dyslipidemia, and asthma. At his last visit three months ago, his doses of metformin and glyburide were optimized. The patient reports that a month later, he experienced an asthma exacerbation and went to the emergency department at a local hospital. His asthma medications were adjusted and he was given oral steroids to control the exacerbation. The oral steroids then caused a significant elevation of his blood glucose levels. When the patient refused to start insulin, providers at the hospital added pioglitazone and acarbose to his outpatient medication regimen to help control his blood glucose. He saw a training resident physician for a hospital follow up visit a week later and was given refills and started on sitagliptin as well. Today, he complains of gastrointestinal pain and bloating with excessive flatulence. This has been bothering him for weeks now, but he is not sure exactly when it began. His asthma is controlled.

Allergies: NKDA

Medications: Metformin 1,000 mg tablet 1 po twice daily with food; glyburide 5 mg tablet two tablets po twice daily with meals; pioglitazone 15 mg tablet 1 po daily; acarbose 25 mg tablet 1 po three times daily with the first bite of each meal; sitagliptin 100 mg tablet 1 po daily; lisinopril 40 mg tablet 1 po daily; atorvastatin 20 mg tablet po every evening; fluticasone/salmeterol 500/50 mcg DPI inhale 1 puff twice daily; albuterol 90 mcg MDI inhale 2 puffs as needed every four to six hours with spacer; prednisone 40 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 208 lb Ht 67 in T 98.6°F BP 132/82 HR 90 RR 14 O_2 sat 99%

Physical exam reveals no wheezes, crackles, rales; no peripheral edema; a bloated abdomen.

A1c 9.7% fasting glucose 248 LDL 76 TG 288 HDL 40 SCr 1.1 K 3.6

The PCP rules out other causes of the GI complaints and suspects a pharmacologic etiology.

Which of the patient's diabetes medications is most likely causing the GI complaints?

Acarbose	Alpha-glucosidase inhibitor (acarbose, miglitol)
Mechanism of Action	Reduces carbohydrate break-down and glucose absorption in the intestinal brush border by inhibiting alpha-glucosidase
***Contraindications/* Precautions**	*Hypersensitivity to the product, inflammatory bowel disease, history or predisposition to bowel obstruction, DKA, cirrhosis; not recommended with renal dysfunction (Scr >2 mg/dL)*/Gas-producing gastrointestinal disorders; may cause LFT elevations at high doses (not common and usually reversible); may cause increased risk of hypoglycemia in combination with sulfonylureas or insulin
Adverse Effects	Flatulence (very common) and bloating, diarrhea, abdominal pain; less common: increased LFT
Drug Interactions	May decrease serum digoxin level
Monitoring	Blood glucose, A1c, initial and periodic renal function, LFT every three months for one year then periodically
Case Notes	Acarbose has a high incidence of flatulence and bloating. Patients will often experience this, and the question is whether they can tolerate the symptoms. While metformin can often cause GI complaints, this is usually diarrhea or general GI upset. The prednisone should have been stopped after several days and once the asthma symptoms had resolved. Pioglitazone may take several weeks to start lowering glucose levels, so this is not an ideal agent for a quick reduction, but is appropriate for long term control. All of the new diabetes medications were added too abruptly and insulin therapy should have been discussed more with the patient. If injectables are truly refused, then the other oral options are individually appropriate. Counsel to take each dose of an alpha-glucosidase inhibitor with the first bite of main meals up to three times daily; skip the dose if the meal is skipped. These agents may lower the A1c by 0.5-0.8 percent. Acarbose dose: 25-100 mg three times daily. Miglitol dose: 25-100 mg three times daily.

A 40-year-old man presents to the pharmacy to pick up refills and new prescriptions called in by his PCP. He has a history of Type 2 diabetes, hypertension, and dyslipidemia. His diabetes is not controlled as evidenced by his fasting glucose levels ranging from 112-150 mg/dL and pre-dinner values ranging from 120-148 mg/dL. However, his two-hour postprandial values are typically <180 mg/dL, and his blood glucose values did improve significantly after recently optimizing his metformin and glyburide doses. The PCP has called in a new prescription for exenatide 5 mcg injected subcutaneously twice daily before meals. The patient explains that he is willing to pick up his metformin refill today, but does not want to start the exenatide because he has an extreme fear of needles and has refused insulin in the past. Two months ago, he had to stop acarbose after a two-week trial, due to GI upset and flatulence with bloating. In the distant past, he also had to stop rosiglitazone due to peripheral edema.

Allergies: NKDA

Medications: Metformin 1,000 mg tablet 1 po twice daily with meals; glyburide 5 mg tablet two tablets po twice daily with meals; pravastatin 20 mg tablet 1 po every evening; lisinopril 40 mg tablet 1 po once daily; hydrochlorothiazide 25 mg tablet 1 po once daily

Physical exam/other studies (reported verbally by the patient):

Wt 202 lb Ht 70 in
Physical exam not performed.
A1c 7.4%

You spend some time discussing diabetes goals with the patient. You also determine that he has already made significant improvements to his diet and is exercising. He is very interested in gaining complete control, but is simply terrified of needles. He would like to try another medication. You decide to call his PCP to recommend another option.

What drug class might you recommend to attain his goal A1c?

Dipeptidyl peptidase IV inhibitor (DPP-IV inhibitor)	Sitagliptin, saxagliptin
Mechanism of Action	Inhibits the DPP-IV enzyme, which results in prolonged incretin activity. Incretin hormones increase glucose-dependent insulin secretion through pancreatic beta cell stimulation, and decrease glucose release from the liver through reduced glucagon release from pancreatic alpha cells. Incretin hormones are normally released in response to a meal and are rapidly inactivated by the DDP-IV enzyme.
***Contraindications*/ Precautions**	*Hypersensitivity to the drug, Type 1 diabetes, DKA/* History of pancreatitis; hypoglycemia; adjust dosing with renal impairment
Adverse Effects	Nausea, hypoglycemia (especially in combination with other diabetes medications), diarrhea, nasopharyngitis, headache, peripheral edema; rarely: acute pancreatitis
Drug Interactions	Sitagliptin may increase serum digoxin levels; saxagliptin levels may be increased by strong CYP3A4/5 inhibitors (limit saxagliptin to 2.5 mg)
Monitoring	Blood glucose, A1c, initial and periodic renal function, pancreatitis
Case Notes	The patient needs a medication added to his current regimen that is capable of lowering the A1c by 0.5%. DPP-IV inhibitors are appropriate for this situation as they may lower the A1c 0.5-0.8%. These drugs are not expected to cause weight gain and may be considered weight neutral. Exenatide would also be an appropriate option in this case if the patient did not have a fear of needles. Other oral product options in this case have already been attempted without success. Counsel patient about recognition, prevention, and treatment of hypoglycemia and to monitor for signs or symptoms of pancreatitis (persistent abdominal pain, nausea, and vomiting). Sitaglipitin is typically dosed 100 mg daily. Lower doses are indicated due to renal impairment (Clcr <50 use 50 mg daily; Clcr <30 use 25 mg daily). Saxagliptin is typically dosed 2.5-5 mg daily; if Clcr <50 or if the patient is taking a CYP 3A4/5 inhibitor, use 2.5 mg daily.

A 42-year-old woman presents to the clinic for a diabetes follow-up visit and is interested in losing weight. She has a past medical history of Type 2 diabetes, heart failure, obesity, and hypertension. Her heart failure is at NYHA Class III based on her recent symptom patterns and is at times unstable. She has been consistently improving her lifestyle and is eating more appropriately in regard to carbohydrates as well as fats, but is not able to tolerate regular exercise. She has seen a significant improvement in her blood glucose levels. At a recent visit, her metformin was stopped due to risks associated with unstable heart failure. Since then, her blood glucose levels have only mildly elevated, but she is not at pre-meal goal values of 70-130 mg/dL. Most of her pre-meal values range from 130-155. She has recently heard of a drug that may help lower her blood glucose levels and also help with weight loss.

Allergies: NKDA

Medications: Glipizide 10 mg tablet 2 po twice daily with meals; lisinopril 40 mg tablet 1 po once daily; metoprolol succinate 100 mg tablet 1 po daily; furosemide 40 mg tablet 1 po twice daily; spironolactone 25 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 330 lb Ht 65 in BP 118/70 HR 64 RR 15

Physical exam reveals an obese female with trace peripheral edema

A1c 7.2% fasting glucose 146 LDL 72 K 4.8 SCr 1.0

You are asked what drug may be appropriate to add to her current regimen to further gain control of her blood glucose levels with a possible benefit of weight loss.

What type of drug do you recommend?

Incretin mimetics (glucagon-like peptide-1 [GLP-1] receptor agonists)	Exenatide, liraglutide
Mechanism of Action	An analog of the GLP-1 incretin hormone. Incretin hormones increase glucose-dependent insulin secretion through pancreatic beta-cell stimulation, decrease glucose release from the liver through reduced glucagon release from pancreatic alpha cells, slow gastric emptying, and decrease food intake.
***Contraindications*/ Precautions**	*Hypersensitivity; Type 1 diabetes; DKA; gastroparesis or other severe GI disease; exenatide is not recommended if Clcr <30 mL/min; do not take liraglutide if history of multiple endocrine neoplasia syndrome type 2 or history/family history of medullary thyroid carcinoma*/History of pancreatitis; use with insulin or secretagogues may increase risk of hypoglycemia; exenatide has been associated with altered renal function from mild to severe, so use caution with history of transplant or Clcr 30-50 mL/min; liraglutide may be associated with thyroid tumors
Adverse Effects	Nausea, vomiting, diarrhea, weight loss (a potential benefit); hypoglycemia (especially in combination with sulfonylureas); rarely: acute pancreatitis, renal dysfunction
Drug Interactions	May decrease absorption of oral medications due to slowed gastric emptying (take drugs with narrow therapeutic index one hour before incretin mimetic), exenatide may increase the anticoagulant effect of warfarin
Monitoring	Blood glucose, A1c, renal function, pancreatitis
Case Notes	The patient needs a medication added to her current regimen that is capable of lowering the A1c by 0.5-1%. Incretin mimetics are appropriate and may cause weight loss. TZDs and metformin are not recommended with her heart failure. Other options may not reduce weight. Initially dose low and gradually increase as tolerated. Administer exenatide within 60 minutes prior to the two main meals of the day at least six hours apart or liraglutide without regard to meals once daily. Exenatide dose: 5-10 mg twice daily. Liraglutide dose: 0.6-1.8 mg once daily.

A 36-year-old woman presents to the pharmacy at 7:30 PM for a refill of her insulins. She has a past medical history of Type 2 diabetes and hypertension. The pharmacy technician that has been working with the patient comes to get you, the pharmacist, because the patient is "acting funny." You immediately notice the patient's hands are shaking and her forehead appears sweaty. As you approach her, she seems to realize that she is experiencing hypoglycemia and retrieves a container of glucose tablets from her purse. Upon checking her blood glucose, she finds a value of 58 mg/dL. About 20 minutes after taking the glucose tablets and resting in a chair, she is feeling better and her glucose has risen to 116 mg/dL. She tells you that two weeks ago, she and her PCP discussed reducing carbohydrate portions from her large dinner-time meal. Ever since then, she has been having low blood glucose levels in the evenings a couple hours after dinner.

Allergies: NKDA

Medications: NPH insulin 36 units subcutaneously before breakfast and 42 units before dinner; regular insulin 22 units subcutaneously 30 minutes before breakfast, and 30 units 30 minutes before dinner; enalapril 10 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 192 lb Ht 66 in BP 148/92 HR 86 RR 16

Physical exam reveals an anxious female with resolving diaphoresis.

After discussing her new diet routine, you determine that her new carbohydrate intake is actually appropriate. To avoid the hypoglycemic episodes, her insulin regimen must be adjusted. You call her PCP's office to make a recommendation.

Which of her four insulin doses would you recommend adjusting?

Regular insulin	Short-acting insulin
Mechanism of Action	Insulin acts to regulate the metabolism of carbohydrate, protein, and fat; it allows for glucose uptake in muscle and adipose tissue. While human insulin is naturally secreted by the pancreas, regular and NPH insulins are manufactured by recombinant-DNA technology.
***Contraindications*/ Precautions**	*Hypersensitivity to regular insulin; administration during hypoglycemia/*May cause hypoglycemia or hypokalemia. Dose may need to be lowered with renal or hepatic impairment.
Adverse Effects	Hypoglycemia, weight gain, injection site reaction, lipoatrophy, lipodystrophy hypokalemia
Drug Interactions	Other glucose-lowering agents or ethanol may increase risk of hypoglycemia; insulin may increase risk of edema when used with thiazolidinediones.
Monitoring	Blood glucose, A1c, potassium
Case Notes	The patient is experiencing hypoglycemia after dinner due to an appropriate change in diet. Based on peak and duration, her evening regular insulin will cover her dinner-time meal and impact glucose values through the evening until bedtime; her evening NPH will cover through the night and impact the morning glucose values. So her evening regular insulin dose needs to be decreased to reduce the risk of hypoglycemia after dinner. Counsel patients that regular insulin must be taken in relation to a meal and optimally 30 to 60 minutes prior; if no meal is eaten, that dose of regular insulin should be skipped. Injection sites should be rotated routinely to avoid lipoatrophy/dystrophy. Patients should carry a quick-acting sugar source to treat any case of hypoglycemia. Regular insulin may be mixed with NPH and should be drawn into the syringe first (clear before cloudy). Do not confuse the U-100 product with the U-500 product. Insulins are categorized based on the onset, peak, and duration of effect as either rapid-, short-, intermediate- or long-acting insulin. Regular insulin: Onset of action in 0.5 hours; Peak effect in 2.5-5 hours; Duration of 14-12 hours.

A 54-year-old man presents to the clinic for a diabetes follow-up visit with his PCP. He has a history of Type 2 diabetes (24 years), hypertension, dyslipidemia, and chronic kidney disease. In the past, his glucose control was maintained with oral glucose-lowering agents, but he is no longer able to take these due to contraindications, adverse effects, and intolerability. He has been fairly well controlled with insulin for several years. He mixes NPH and regular insulin and injects the dose twice daily, 30 minutes prior to breakfast and dinner (evening meal). He records his blood glucose four times a day, before each meal and at bedtime. Recently, he has had to stop his mid-day exercise routine due to a back injury. Before breakfast and lunch, his blood glucose values have mostly been at goal between 70-130 mg/dL. Before dinner, his blood glucose values have risen and are averaging 150 mg/dL. His bedtime values have remained acceptable at 100-140 mg/dL.

Allergies: Sulfa (difficulty breathing)

Medications: NPH insulin inject 52 units subcutaneously before breakfast and 62 units before dinner; regular insulin inject 36 units subcutaneously 30 minutes before breakfast, and 48 units 30 minutes before dinner; lisinopril 40 mg tablet 1 po daily; pravastatin 20 mg tablet po every evening; aspirin 81 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 222 lb Ht 72 in T 98.6°F BP 122/74 HR 78 RR 16

Physical exam reveals no pertinent findings.

A1c 7.1% fasting glucose 107 LDL 92 TG 152 HDL 40 SCr 1.6 K 4.2

You are working with the PCP today and providing pharmacotherapy recommendations. You decide, based on recent blood glucose patterns, to recommend adjusting one of the patient's four insulin doses.

Which of his four insulin doses will you adjust to improve his pre-dinner glucose values?

NPH insulin	Intermediate-acting insulin
Mechanism of Action	Insulin acts to regulate the metabolism of carbohydrate, protein, and fat; it allows for glucose uptake in muscle and adipose tissue. While human insulin is naturally secreted by the pancreas, regular and NPH insulins are manufactured by recombinant-DNA technology.
***Contraindications*/ Precautions**	*Hypersensitivity to NPH insulin*/May cause hypoglycemia or hypokalemia. Dose may need to be lowered with renal or hepatic impairment.
Adverse Effects	Hypoglycemia, weight gain, injection site reaction, hypokalemia, lipoatrophy, lipodystrophy
Drug Interactions	Other glucose-lowering agents may increase risk of hypoglycemia; insulin may increase risk of edema when used with thiazolidinediones.
Monitoring	Blood glucose, A1c, potassium
Case Notes	The patient is experiencing an increase in his pre-dinner glucose levels due to a discontinuation of mid-day exercise. His current insulin regimen has been effective as evidenced by his A1c, which is slightly above the ADA goal of <7 percent (likely increased due to this recent history). Based on peak and duration, his morning regular insulin will cover his breakfast and impact the pre-lunch glucose values; his morning NPH will cover his lunch and impact the pre-dinner glucose values. So his morning NPH dose needs to be increased to lower the pre-dinner glucose elevations. Injection sites should be rotated routinely to avoid lipoatrophy/dystrophy. Patients should carry a quick-acting sugar source to treat any case of hypoglycemia. Regular insulin or any rapid-acting insulin (aspart, lispro, or glulisine) may be mixed with NPH and should be drawn into the syringe first (clear before cloudy). Insulins are categorized based on the onset, peak, and duration of effect as either rapid-, short-, intermediate- or long-acting insulin. NPH: Onset of action in one to two hours; Peak effect in 4-12 hours; Duration of 14-24 hours.

A 32-year-old woman presents to her family medicine clinic for a hospital follow-up visit six weeks after an admission to a local hospital where she was diagnosed with Type 2 diabetes. She had only occasionally visited her PCP in the past and this new diagnosis of diabetes is her only outstanding past medical history. She complains of blurry vision, increased thirst, and increased urinary frequency. Her pre-meal blood glucose readings (breakfast, lunch, and dinner) from her home glucometer are all in the 300-400s (mg/dL). She is compliant with her insulin regimen that was started in the hospital, but is very concerned that she is not getting better.

Allergies: NKDA

Medications: Insulin glargine 40 units subcutaneously every evening; insulin lispro subcutaneously per sliding scale (200-249 = 2 units; 250-299 = 3 units; 300-349 = 4 units; 350-399 = 5 units; ≥ 400 = 6 units)

Physical Exam/Other Studies:

Wt 248 lb Ht 65 in BP 128/32 HR 78 RR 14

Urine ketone negative

Physical exam reveals an obese female distressed over uncontrolled diabetes.

The PCP requests a pharmacotherapy consult with the clinical pharmacist. You determine that the patient has appropriate insulin injection technique and has started improving her diet. Her blood glucose levels have not improved since her hospital discharge.

What would be the most appropriate insulin to adjust at this time?

Insulin lispro	Rapid-acting (bolus) insulin (insulin lispro, insulin aspart, insulin glulisine)
Mechanism of Action	Insulin acts to regulate the metabolism of carbohydrate, protein, and fat; it allows for glucose uptake in muscle and adipose tissue. While human insulin is naturally secreted by the pancreas, rapid and long-acting insulins are manufactured and known as analogues.
***Contraindications*/ Precautions**	*Hypersensitivity to insulin product; administration during hypoglycemia*/May cause hypoglycemia or hypokalemia. Dose may need to be lowered with renal or hepatic impairment.
Adverse Effects	Hypoglycemia, weight gain, injection site reaction, lipoatrophy, lipodystrophy hypokalemia
Drug Interactions	Other glucose-lowering agents or ethanol may increase risk of hypoglycemia; insulin may increase risk of edema when used with thiazolidinediones.
Monitoring	Blood glucose, A1c, potassium
Case Notes	The patient was started on a set dose of long-acting insulin and rapid-acting insulin dosed by a sliding scale. While sliding scales are often used to start insulin regimens, they are often not ideal for long-term pattern management. Solely using a sliding scale approach does not prevent glucose elevations day to day, but instead treats elevations as they occur. Without adjusting doses based on daily blood glucose patterns, control may not be achieved. This patient should be put on a set dose of rapid insulin at each meal and titrated to appropriate doses to achieve goal pre- and post-meal glucose values. Counsel patient that rapid insulin must be taken in relation to a meal and optimally one to five minutes prior; if no meal is eaten, that dose of rapid insulin should be skipped. Injection sites should be rotated routinely to avoid lipoatrophy/dystrophy. Patients should carry a quick-acting sugar source to treat any case of hypoglycemia. Insulins and are categorized based on the onset, peak, and duration of effect as either rapid-, short-, intermediate- or long-acting insulin. Rapid insulin: Onset of action in 0.2-0.5 hours; Peak effect in 0.5-2.5 hours; Duration of up to five hours.

A 21-year-old man returns to the diabetes clinic for a routine diabetes follow-up visit. He has a past medical history of Type 1 diabetes. He has been generally well controlled for several years and is very compliant with diet and exercise habits as well as his medications and blood sugar monitoring. He eats approximately 45-60 g of carbohydrates consistently at each of three meals daily. He also eats appropriate snacks of foods containing 15-30 g of carbohydrate between meals and has never needed a consistent evening snack. His current insulin regimen was determined using pre-meal blood glucose pattern management and has been stable for months. He uses occasional correction doses of his rapid insulin for modest glucose excursions. His recent blood glucose log reveals morning fasting glucose levels averaging 160 mg/dL, which is higher than usual for him. His other pre-meal glucose values are all generally in the goal range of 70-130 mg/dL and the patient denies hypoglycemia. His injection technique is appropriate. He eats meals at 7 AM, noon, and 6 PM

Allergies: Sulfonamides (rash)

Medications: Insulin glargine 30 units subcutaneously every evening; insulin aspart 6 units subcutaneously before breakfast, 8 units before lunch, and 10 units before dinner

Physical Exam/Other Studies:

Wt 150 lb Ht 71 in BP 116/72 HR 70 RR 12

Urine ketone negative

Physical exam reveals a well developed, well nourished male in no acute distress.

You are the clinical pharmacist on a multidisciplinary team of providers in the diabetes clinic. You have interviewed the patient and are about to discuss treatment options with the endocrinologist.

Which of the patient's four insulin doses would be most appropriate to adjust to address his elevated morning blood glucose levels?

Insulin glargine	Long-acting (basal) insulin (insulin glargine, insulin detemir)
Mechanism of Action	Insulin acts to regulate the metabolism of carbohydrate, protein, and fat; it allows for glucose uptake in muscle and adipose tissue. While human insulin is naturally secreted by the pancreas, rapid and long-acting insulins are manufactured and known as analogues.
***Contraindications*/ Precautions**	*Hypersensitivity to the insulin product; administration during hypoglycemia*/May cause hypoglycemia or hypokalemia. Dose may need to be lowered with renal or hepatic impairment.
Adverse Effects	Hypoglycemia, weight gain, injection site reaction, lipoatrophy, lipodystrophy hypokalemia,
Drug Interactions	Other glucose-lowering agents or ethanol may increase risk of hypoglycemia; insulin may increase risk of edema when used with thiazolidinediones.
Monitoring	Blood glucose, A1c, potassium
Case Notes	Insulin glargine is the only insulin that should be actively working to lower blood glucose levels through the night to have a significant impact on the morning fasting levels. Rapid pre-meal insulin should work to cover each respective meal and impact blood glucose levels over the next four to five hours after meals. Since glargine will impact glucose levels for 24 hours, it may be necessary to reduce some rapid insulin doses to avoid hypoglycemia. Counsel patients that long-acting insulin may be taken without regard to meals and is often dosed at bed time (can be taken any time of day). Rotate injection sites routinely to avoid lipoatrophy/dystrophy. Long-acting insulin may not be mixed in a syringe with other insulins. Insulins are categorized based on the onset, peak, and duration of effect as either rapid-, short-, intermediate- or long-acting insulin. Long-acting insulin: Onset of action in three to four hours; glargine has no peak effect; detemir has a peak effect in three to nine hours; duration of glargine is generally 24 hours; duration of detemir varies from 6-23 hours and is dependent on dose (lower doses of 0.1-0.2 units/kg/day have 5.7-12.1 hour duration while high doses of ≥0.8 units/kg/day have 22-23 hour duration).

A 35-year-old woman presents to your pharmacy wanting to transfer all of her prescriptions to your store. She explains that she recently moved to this area from across town. After calling the other pharmacy and successfully transferring the prescriptions, you spend time gathering some history from the patient. The patient reports that she has had Type 1 diabetes for 30 years and has even developed some diabetes complications that you correctly interpret as neuropathy and gastroparesis. She also has hypertension and dyslipidemia.

Allergies: Aspirin (rash)

Medications: Insulin glargine 30 units subcutaneously every evening; insulin glulisine 8 units subcutaneously immediately before each main meal three times daily; pramlintide 30 mcg subcutaneously before each main meal three times daily; metoclopramide 10 mg tablet 1 po four times daily with meals and at bedtime; lisinopril 40 mg tablet 1 po daily; hydrochlorothiazide 25 mg tablet 1 po daily; lovastatin 40 mg tablet 1 po every evening

Physical Exam/Other Studies:

Wt 148 lb Ht 64 in BP 108/72 HR 72

No labs are available at this time.

The patient complains of frequent nausea. She can't eat very much food because she "gets full" so easily and just doesn't feel like eating. As a result, she often skips meals. Her blood glucose levels have been very erratic with many high readings mixed with low readings. She said this all started a few months ago when some new medications were added to her regimen.

After assessing her medications and her recent history, you realize that there is a contraindication against the use of one of her medications. You tell her that you are going to call her PCP to discuss stopping one of her drugs.

Which drug should you recommend stopping at this time?

Pramlintide	Amylin mimetic (amylinomimetic)
Mechanism of Action	Pramlintide is a synthetic analog of human amylin. Amylin is secreted with insulin from pancreatic beta cells; it reduces postprandial glucose elevations through prolonged gastric emptying, reduced postprandial glucagon secretion, and centrally-mediated appetite suppression
***Contraindications*/ Precautions**	*Hypersensitivity to pramlintide, gastroparesis, or hypoglycemia unawareness*/Conditions or concurrent medications likely to impair gastric motility or in patients requiring medication to stimulate gastric emptying; history of nausea; neuropathic conditions which may mask signs/symptoms of hypoglycemia
Adverse Effects	Nausea, vomiting, anorexia, headache, severe hypoglycemia
Drug Interactions	Concurrent use of other glucose-lowering agents, especially insulin, may increase risk of hypoglycemia; may enhance GI effects of anticholinergic drugs; ethanol, garlic, chromium
Monitoring	Blood glucose, A1c, hypoglycemia history
Case Notes	Pramlintide is contraindicated for use if a patient has a diagnosis of gastroparesis. It may further slow gastric emptying time and worsen this neuropathy. It is possible that the metoclopramide had been controlling the gastroparesis until the pramlintide was added a few months ago. Her nausea could also be from the pramlintide. Once she is able to eat regularly again and resume regular insulin doses, her erratic blood glucose levels may stabilize. Then insulin adjustments can be made to regain control. Dosing in Type 1 diabetes is 15-60 mcg immediately prior to meals. Dosing in Type 2 diabetes is 60-120 mcg immediately prior to meals. When initiating pramlintide, reduce current insulin dose by 50 percent to avoid hypoglycemia. Counsel patient about recognition, prevention, and treatment of hypoglycemia. Do not mix with insulin; inject subcutaneously in abdomen or thigh separate from insulin injection sites; rotate injection sites regularly. Do not use insulin syringes to administer dose as it is not measured in "units."

A 46-year-old woman presents to her physician complaining of feeling tired, lethargic, and not being able to think straight for the past four months. She also mentions that she is always turning the heat up at home while her husband is sitting around in a t-shirt. She wonders if maybe she is starting to go through menopause and would like a medication to help her have more energy. She has no other medical conditions that she is aware of at this time.

Allergies: Penicillin (rash)

Medications: None

Physical Exam/Other Studies:

Wt 165 lb Ht 65 in T 97.1°F BP 141/78 HR 63 RR 16 O_2 sat 98%

Physical exam reveals dry skin, periorbital edema, and a normal thyroid gland.

TSH 10.1 FT_4 0.65

She is given a diagnosis of hypothyroidism

What is the best treatment for her hypothyroidism?

Levothyroxine	Thyroid products (levothyroxine, liothyronine, liotrix, desiccated thyroid)
Mechanism of Action	Levothyroxine (T_4) is a synthetic form of thyroxine, an endogenous hormone secreted by the thyroid gland. T_4 is converted to its active metabolite, L-triiodothyronine (T_3). Thyroid hormones (T_4 and T_3) then bind to thyroid receptor proteins in the cell nucleus and exert metabolic effects through control of DNA transcription and protein synthesis.
***Contraindications*/ Precautions**	*Hypersensitivity to the agent, acute myocardial infarction, thyrotoxicosis, uncorrected adrenal insufficiency*/ Do not use for weight reduction or benign thyroid nodules, use with caution in patients with cardiovascular disease, adrenal insufficiency, diabetes mellitus or insipidus, myxedema, osteoporosis, and the elderly
Adverse Effects	Angina, arrhythmias, heart failure, choking with the Levoxyl® brand
Drug Interactions	Bile acid sequestrants, calcium polystyrene sulfonate, calcium salts, carbamazepine, estrogen derivatives, iron salts, orlistat, phenytoin, raloxifene, rifampin, sevelamer, sodium iodide 131, sodium polystyrene sulfonate, sucralfate, theophylline, and vitamin K antagonists
Monitoring	Thyroid function tests (TSH), heart rate, blood pressure, signs/symptoms of hypothyroidism and hyperthyroidism
Case Notes	Thyroid replacement therapy is the mainstay for the treatment of hypothyroidism. Levothyroxine is the most commonly used thyroid product due to its chemical stability, low cost, uniform potency, and low degree of antigenicity compared to desiccated thyroid. The typical dosing range is 12.5-300 mcg/day depending on the severity of the hypothyroidism. Elderly patients and those with cardiovascular disease should be initiated on low doses and slowly titrated to the effective dose. Patient medication profiles should be reviewed carefully due to the numerous drug interactions indicated above. Levothyroxine is the drug of choice for treating hypothyroidism in pregnancy and is pregnancy category A.

A 30-year-old woman presents to her physician complaining of palpitations, anxiety, diarrhea, and weight loss that has been progressively getting worse over the past several months. She also mentions that she has not been getting her menstrual periods for about the same time period. Her past medical history is unremarkable.

Allergies: Sulfa (rash)

Medications: None

Physical Exam/Other Studies:

Wt 135 lb Ht 65 in T 99.1°F BP 138/80 HR 140 RR 20 O_2 sat 98%

Physical exam reveals fine hair, positive lid lag, mild proptosis, enlarged thyroid with a positive bruit, tachycardia, and a fine tremor when her hands are outstretched.

TSH < 0.01 FT_4 7.3 TT_4 15

She is given a diagnosis of hyperthyroidism—likely Graves disease.

In addition to propranolol to control her heart rate, and until she decides whether she wants surgery or radioactive iodine treatment, what medication could be prescribed to possibility help her achieve remission of her hyperthyroidism?

Thioamides	Methimazole, propylthiouracil
Mechanism of Action	Inhibits the synthesis of thyroid hormones by blocking the oxidation of iodine in the thyroid gland thus inhibiting the combination of iodine and tyrosine to form thyroxine and triiodothyronine. Propylthiouracil also blocks the synthesis of thyroxine to triiodothyronine.
***Contraindications*/ Precautions**	*Hypersensitivity to the agent*/Bleeding, bone marrow suppression, dermatitis, hepatotoxicity (black box warning for propylthiouracil), fever, lupus-like syndrome, vasculitis, nephritis (propylthiouracil), pneumonitis (propylthiouracil)
Adverse Effects	Rash, fever, and rarely: agranulocytosis, acute liver failure
Drug Interactions	May diminish the effects of radioactive iodide, and must be discontinued two to three days prior to treatment. May diminish the anticoagulant effect of the vitamin K antagonists.
Monitoring	CBC with differential, prothrombin time, liver function tests, bilirubin, thyroid function tests
Case Notes	The thioamides are prescribed in an attempt to achieve remission in hyperthyroidism although remission rates are variable and relapses are frequent. Remission is more likely if mild hyperthyroidism is present or with small goiters. They are used first-line in children, adolescents, and in pregnancy. Although both agents are pregnancy category D, the treatment of hyperthyroidism in pregnancy is necessary to avoid adverse effects to both the mother and the fetus. Propylthiouracil is often preferred in the first trimester of pregnancy since methimazole has been associated with the occurrence of birth defects. Thioamides are also used as initial treatment in severe cases and in the preoperative preparation prior to thyroidectomy. Elderly patients or patients with cardiac manifestations may require pretreatment with antithyroid medications prior to radioactive iodine use. The dose of propylthiouracil in adults is 100-900 mg/day while the methimazole dose is typically 5-60 mg/day depending on the severity of the hyperthyroidism.

A 48-year-old woman presents to her physician complaining of palpitations, diarrhea, and weight loss that has been progressively getting worse over the past several months. She is diagnosed with hyperthyroidism and scheduled to undergo radioactive iodine treatment. Her past medical history is unremarkable.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 145 lb Ht 67 in T 96.1°F BP 128/78 HR 125 RR 18 O_2 sat 98%

Physical exam reveals fine hair, mild proptosis, enlarged thyroid with a positive bruit, and tachycardia.

TSH < 0.01

What medication could be prescribed temporarily to help inhibit thyroid hormone release following her radioactive iodine treatment?

Iodides	Potassium iodide
Mechanism of Action	Inhibits the secretion of thyroid hormones and fosters colloid accumulation in thyroid follicles. Following exposure to radioactive iodine, it blocks the uptake and decreases the risk of thyroid cancer.
***Contraindications*/ Precautions**	*Hypersensitivity to iodine or any component of the formulation; dermatitis herpetiformis, hypocomplementemic vasculitis, nodular thyroid condition with heart disease*/Hypothyroidism, skin reactions, use with caution in adrenal insufficiency, bronchitis, cardiovascular disease, cystic fibrosis, myotonia congenital, renal impairment, thyroid disease, and tuberculosis
Adverse Effects	Irregular heartbeat, hypersensitivity reactions, salivary gland swelling, metallic taste, burning mouth and throat, sore teeth and gums, diarrhea
Drug Interactions	Use with caution with agents that increase potassium; may enhance the toxic effects of lithium; may diminish the anticoagulant effects of vitamin K antagonists
Monitoring	Thyroid function tests and signs/symptoms of hyperthyroidism
Case Notes	The iodides are used to acutely block the thyroid hormone release through the Wolff-Chaikoff effect and to decrease the size and vascularity of the gland. Patients should experience symptom improvement in two to seven days, but the effect may only last a few weeks before the thyroid gland escapes the effect. The iodides are often used in preparing a patient with Graves disease for surgery, in severely thyrotoxic patients, or to inhibit hormone release following radioactive iodine treatment. The dosing varies depending on the product selected. Doses of 6-8 mg/day have been demonstrated to be effective, but often much higher doses are used.

A 30-year-old man enters the pharmacy and approaches you, the pharmacist, for advice. He complains of mild heartburn after larger meals over the past few days. The episodes seem to be more of a nuisance to the patient rather than a consistently bothersome concern and he rates the pain as 1-2 on a scale of 10. He reports no significant medical history, but upon your questioning believes he may have occasional constipation, which is unrelated to his current complaint. He has not tried anything yet to treat the heartburn symptoms and wants to try a product for some relief.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:
None performed

You determine that the patient's symptoms are mild and intermittent.

What OTC medication can you recommend to quickly relieve his intermittent bouts of heartburn?

Magnesium Hydroxide	Antacid; magnesium salt; laxative
Mechanism of Action	Reacts with hydrochloric acid in the stomach to form magnesium chloride and increases gastric pH; osmotic retention of fluid may increase peristaltic activity and promote bowel movements.
***Contraindications*/ Precautions**	*Hypersensitivity*/Renal impairment (may cause magnesium accumulation); use caution with neuromuscular disease; see physician if GI symptoms persist for more than two weeks of treatment
Adverse Effects	Diarrhea, hypermagnesemia in renal failure
Drug Interactions	Antacids may decrease absorption of quinolone antibiotics, tetracycline, nitrofurantoin, and isoniazid; antacids may decrease the absorption of medications requiring an acidic environment such as iron supplements, ketoconazole, itraconazole, sucralfate, calcium carbonate, levothyroxine; excessive risk of diarrhea if used with misoprostol; see product labeling for numerous interactions.
Monitoring	Efficacy and adverse effects
Case Notes	Mild intermittent heartburn can be treated with antacids alone or in combination with H_2 receptor antagonists; mild GERD can be treated with H_2 receptor antagonists or proton pump inhibitors (PPI); moderate to severe GERD should be treated with PPIs. Because of the patient's occasional constipation, magnesium hydroxide is an appropriate choice for his mild heartburn. Without his constipation, calcium carbonate or aluminum hydroxide products would be options. Counsel patient to drink eight ounces of water with each dose. Separate from interacting medications by two hours. Available as a liquid or tablet; dose the 400 mg/5 mL liquid product at 5-15 mL up to four times daily as needed; dose the 311 mg tablet product at two to four tablets every four hours up to four times daily.

A 58-year-old man presents to the pharmacy complaining of mild to moderate heartburn symptoms about two to three times a week that do not completely respond to antacids. He has a past medical history of hypertension, dyslipidemia, and coronary artery disease (he had a coronary stent placed five months ago).

Allergies: NKDA

Medications: Metoprolol succinate 100 mg tablet po once daily; ramipril 10 mg tablet po once daily; atorvastatin 80 mg tablet po once every evening; clopidogrel 75 mg tablet po once daily; aspirin 81 mg tablet (OTC) po once daily

The patient has made an appointment to see his PCP, but the visit is three weeks away. He is asking for you to recommend something he can take over-the-counter to help relieve his symptoms.

Physical Exam/Other Studies:

None performed

What drug or drug class would you recommend to safely relieve his heartburn?

H_2 Receptor Antagonists	Cimetidine (po, IV), famotidine (po, IV), nizatidine (po), ranitidine (po, IV)
Mechanism of Action	Reversibly compete with histamine at the H_2 receptor sites in the parietal cell of the stomach to inhibit acid secretion
***Contraindications*/ Precautions**	*Hypersensitivity/*Renal impairment, B_{12} deficiency, see physician if GI symptoms persist for more than two weeks of treatment
Adverse Effects	Headache, dizziness, confusion in the elderly, rare hematologic abnormalities
Drug Interactions	Drugs requiring an acidic environment for absorption (eg, ketoconazole, itraconazole, sucralfate, iron supplements, calcium carbonate, levothyroxine); cimetidine inhibits CYP1A2, 2C9, 2C19, 2D6, 2E1, and 3A4 and will interact with many drugs, including theophylline, phenytoin, and warfarin
Monitoring	CBC, LFT, renal function for dosing
Case Notes	Mild intermittent heartburn can be treated with antacids alone or in combination with H_2 receptor antagonists; mild GERD can be treated with H_2 receptor antagonists or proton pump inhibitors (PPIs); moderate to severe GERD should be treated with PPIs. In this case, the heartburn is not responding to antacids, and it is advised to avoid PPIs in combination with clopidogrel due to risk of reducing antiplatelet activity (this has been observed with omeprazole as an inhibitor of CYP2C19; it is advised to avoid cimetidine since it also inhibits CYP2C19). So, an H_2 receptor antagonist could be recommended in this case of mild to moderate heartburn. Ranitidine dosing for prevention of heartburn: ranitidine (OTC) 75 mg tablet po 30-60 minutes before eating food or drinking beverages that cause heartburn (no more than 150 mg a day). Ranitidine dosing for treating GERD: 150 mg twice daily. Famotidine (OTC) labeling for heartburn: 10-20 mg every 12 hours; dose may be taken 15-60 minutes before eating foods known to cause heartburn. Adjust dosing with renal impairment for any H_2 receptor antagonist.

A 48-year-old woman presents to her PCP's office with a complaint of midepigastric pain that often awakens her at night. It has been present the past few months. The pain is described as burning, like heartburn, and often relieved by antacids. It sometimes occurs a couple of hours after meals accompanied by nausea, but not consistently. She has a past medical history of hypertension, allergic rhinitis, and depression.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; lisinopril 10 mg tablet 1 po daily; sertraline 100 mg tablet 1 po daily; calcium carbonate 1,000 mg tablet (OTC) 2-3 po as needed for GI symptoms and not more than seven tablets in 24 hours

Physical Exam/Other Studies:

Wt 152 lb Ht 70 in T 98.6°F BP 144/86 HR 84 RR 14 O_2 sat 99%
Physical exam reveals mild epigastric tenderness.
Hemoccult positive.
H. pylori antibody positive on fingerstick.
Upper endoscopy ordered.

The patient is diagnosed with peptic ulcer disease (PUD) and is started on clarithromycin 500 mg tablet 1 po twice daily and amoxicillin 500 mg capsule 2 po twice daily.

A drug from what other class needs to be added to complete this 14-day, three-drug regimen to treat PUD and eradicate *H pylori*?

Proton Pump Inhibitor (PPI)	Esomeprazole (po/IV), dexlansoprazole (po), lansoprazole (po), omeprazole (po), pantoprazole (po/IV), rabeprazole (po)
Mechanism of Action	Suppresses gastric acid secretion by irreversibly inhibiting the parietal cell H^+/K^+ ATP pump
***Contraindications*/ Precautions**	*Hypersensitivity to the medication*/PPIs may reduce the antiplatelet effect of clopidogrel, which may increase cardiovascular risks.
Adverse Effects	Headache, nausea, vomiting, diarrhea, increased risk of osteoporosis-related bone fractures
Drug Interactions	Clopidogrel, drugs requiring an acidic environment for absorption (eg, ketoconazole, itraconazole, sucralfate, iron supplements, calcium carbonate, levothyroxine); omeprazole induces CYP1A2 and inhibits CYP 2D6, 2C9, 2C19, and 3A4
Monitoring	Efficacy
Case Notes	First-line therapy for *H. pylori*-positive PUD is a 7-14 day course of a PPI-based three-drug regimen of a PPI plus clarithromycin, plus either amoxicillin or metronidazole. Second-line therapy includes a four-drug regimen of a PPI plus bismuth subsalicylate, plus metronidazole, plus tetracycline or amoxicillin or clarithromycin. Do not crush or chew PPI oral products. PPIs may also be indicated for heartburn, gastric ulcer, duodenal ulcer, GERD, erosive esophagitis, or hypersecretory conditions, each with specific dosing. For *H pylori* eradication, dosing varies depending on different drug-regimen combinations. Omeprazole: 20-40 mg once daily or divided twice daily. Lansoprazole: 30 mg two to three times daily (depending on regimen combination). Pantoprazole: 40 mg twice daily. Rabeprazole: 20 mg twice daily. Esomeprazole: 40 mg once daily. Dexlansoprazole is not currently indicated for *H pylori* eradication.

A 53-year-old man returns to his PCP's office for a follow-up visit for the treatment of his active, *H pylori*-positive, peptic ulcer disease (PUD). Three weeks ago, he completed a seven-day course of omeprazole, clarithromycin, and amoxicillin. His PUD symptoms slightly improved, but he still suffers from significant epigastric pain with night awakenings. His past medical history includes PUD and hypertension.

The patient is referred to a gastroenterologist who performs an upper endoscopy procedure. He is able to view the ulcer and gets a biopsy for rapid urease test.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; amlodipine 10 mg tablet 1 po daily; calcium carbonate 1,000 mg tablet (OTC) 2-3 po as needed for GI symptoms and not more than seven tablets in 24 hours

Physical Exam/Other Studies:

Wt 244 lb Ht 72 in T 98.6°F BP 148/94 HR 76 RR 12 O_2 sat 98%

Physical exam reveals epigastric tenderness.

Rapid urease test is positive for *H pylori*.

The patient needs a second treatment for his PUD. It is decided to use a four-drug regimen, and he is started on omeprazole 40 mg capsule, one po twice daily; metronidazole 500 mg tablet, one po twice daily; and tetracycline 500 mg capsule, one po four times daily.

A drug from what other class needs to be added to complete this 14-day, four-drug regimen to treat PUD and eradicate *H pylori*?

Bismuth Subsalicylate	Bismuth
Mechanism of Action	The bismuth moiety acts as an antimicrobial against bacterial and viral gastrointestinal pathogens, while the salicylate moiety acts as an antisecretory agent.
***Contraindications*/ Precautions**	*Hypersensitivity to the medication; allergy to aspirin or salicylates; history of severe GI bleed or coagulopathy; pregnancy; do not use in children or teenagers with influenza or chickenpox due to risk of Reye's syndrome/*Renal impairment, concomitant aspirin use
Adverse Effects	Confusion, anxiety, neurotoxicity, discoloration of the tongue, hearing loss, tinnitus
Drug Interactions	May decrease absorption of tetracycline derivatives
Monitoring	Look for adverse effects. Tinnitus could be a sign of toxicity.
Case Notes	First-line therapy for *H pylori*-positive PUD is a 7-14 day course of a PPI-based three-drug regimen of a PPI plus clarithromycin, plus either amoxicillin or metronidazole. Second-line therapy includes a four-drug regimen of a PPI plus bismuth subsalicylate, plus metronidazole, plus either tetracycline, amoxicillin, or clarithromycin. Second-line therapy used to treat a failed first therapy should be continued for 14 days and use different antibiotics than the first trial. Bismuth may discolor the tongue and darken stools.

A 40-year-old man presents to his PCP for a follow-up visit regarding his recently treated peptic ulcer. The patient has a past medical history of PUD and low back pain. He reports that he has never been able to swallow "pills" and it was very difficult for him to complete the 14-day treatment of triple-agent therapy for his PUD. He has used a children's ibuprofen suspension around the clock for 10 years for his back pain and refuses to stop or switch to acetaminophen.

Allergies: NKDA

Medications: Ibuprofen suspension 100 mg/5 mL (OTC) 20-40 mL every eight hours as needed for back pain

Physical Exam/Other Studies:

Wt 180 lb Ht 70 in T 98.6°F BP 128/82 HR 76 RR 12 O_2 sat 99%

Physical exam reveals no pertinent findings.

Hemoccult negative.

H pylori negative.

The patient is at risk for an NSAID-induced ulcer, and it is decided that he needs prophylaxis to maintain his healed duodenal ulcer. He refuses to take a routine tablet or capsule.

What drug is available as a liquid that may be used in this patient?

Sucralfate	Miscellaneous gastrointestinal agent
Mechanism of Action	Forms a protein complex that coats and protects the gastric lining from peptic acid, pepsin, and bile salts
***Contraindications*/ Precautions**	*Hypersensitivity to the medication*/Renal impairment, altered absorption of other medications
Adverse Effects	Constipation, rarely bezoar formation
Drug Interactions	Aluminum-, calcium-, and magnesium-containing products (antacids) interfere with sucralfate action and should be avoided 30 minutes before or after sucralfate. Concomitant use with fluoroquinolones, phenytoin, digoxin, theophylline, quinidine, amitriptyline, warfarin, and ketoconazole may reduce their bioavailability.
Monitoring	Adverse effects
Case Notes	Sucralfate is available as a liquid and indicated for maintenance of the patient's ulcer. PPIs are preferred and are more effective. An alternative could have been to use an extemporaneously prepared PPI product that could be swallowed with applesauce or a PPI product that orally disintegrates (lansoprazole; Prevacid SoluTab). Take sucralfate on an empty stomach. To reduce risk of decreasing absorption of other drugs, take other drugs at least two hours before or four to six hours after sucralfate doses. Maintenance/prophylaxis dose for duodenal ulcer is 1 g twice daily. Store suspension at room temperature and shake well before use.

A 67-year-old man presents to his PCP's office to follow up on his osteoarthritis (OA). He has a past medical history of OA, diabetes, hypertension, and dyslipidemia. He has been taking NSAIDs to successfully control his OA for several years, but recently his PCP increased his NSAID dose to maintain full control. Since then, his OA has been asymptomatic, but he has complaints of occasional heartburn and dyspepsia. He wishes to continue his NSAID use.

Allergies: NKDA

Medications: Aspirin 81 mg tablet (OTC) 1 po daily; metformin 1,000 mg tablet 1 po twice daily; insulin glargine 20 units subcutaneously every evening; ramipril 5 mg tablet 1 po daily; atorvastatin 20 mg tablet 1 po every evening; diclofenac 75 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 165 lb Ht 69 in T 98.6°F BP 116/76 HR 76 RR 14 O_2 sat 99%

Physical exam reveals no pertinent findings.

A1c 6.7% LDL 66 TG 152 HDL 56 SCr 1.0 K 4.1

The patient is considered high risk for an NSAID-induced ulcer based on risk factors of age >65, aspirin use, and high-dose NSAID use. It is decided that he needs prophylaxis to avoid development of an NSAID-induced ulcer.

What drug can be added to his current regimen to help reduce his risk of NSAID-induced ulcer?

Misoprostol	Prostaglandin
Mechanism of Action	As a synthetic prostaglandin E_1 analog, it replaces protective prostaglandins that NSAID use has reduced; has also been shown to induce uterine contractions.
***Contraindications*/ Precautions**	*Hypersensitivity to the medication, pregnancy (category X)*/Renal impairment, cardiovascular disease; not to be used to reduce NSAID-induced ulcers in women of childbearing potential unless woman is capable of complying with effective contraceptive measures
Adverse Effects	Constipation, diarrhea, nausea, abdominal pain, headache, gynecologic disorders (cramps, dysmenorrhea, hypermenorrhea, spotting, postmenopausal vaginal bleeding, and other menstrual disorders)
Drug Interactions	Magnesium-containing antacids should be avoided as they enhance the adverse effects of misoprostol. Misoprostol may enhance the therapeutic effect of carbetocin, and concomitant use should be avoided.
Monitoring	Investigate any abnormal vaginal bleeding.
Case Notes	Misoprostol is appropriate to add to the patient's current NSAID therapy to help protect the gastric lining. It would also be appropriate to add a PPI to his NSAID therapy instead of misoprostol. Misoprostol is dosed 100-200 mcg tablet four times daily with food; dose may be reduced to avoid diarrhea, but may not be effective at 400 mcg or less per day. This drug may cause severe fetal defects, miscarriage, or abortion; counsel patients to not share medication with others. It may be used for medical termination of pregnancy of ≤49 days (in conjunction with mifepristone). Misoprostol also has a role in induction of labor in pregnancy.

A father enters your pharmacy asking for an OTC product for motion sickness. He and his son are traveling, and the 14-year-old boy has become nauseated by the curving roads in the region. The teenager has no significant past medical history and takes no regular medication.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:
None available

After a discussion with the father, you rule out other potential causes of this simple nausea, such as food poisoning, and make a recommendation.

What type of agent should be recommended for motion sickness?

Antihistamine-Anticholinergic Drugs	Cyclizine, dimenhydrinate, diphenhydramine, meclizine
Mechanism of Action	Anticholinergic action blocks the chemoreceptor trigger zone
***Contraindications*/Precautions**	*Hypersensitivity*/Asthma, glaucoma, BPH, pyloric/duodenal obstruction, elderly may be more sensitive to adverse effects, caution driving or operating machinery
Adverse Effects	Drowsiness, thickening of bronchial secretions, headache, dizziness, xerostomia, blurred vision, constipation
Drug Interactions	Alcohol, anticholinergic agents, acetylcholinesterase inhibitors, amphetamines, CNS depressants, pramlintide, betahistine
Monitoring	Monitor for adverse effects and efficacy.
Case Notes	For "simple" nausea such as motion sickness, intermittent use of antihistamine-anticholinergic drugs is often effective. Elderly may be more susceptible to anticholinergic effects. Meclizine is indicated for adults and children over 12 years of age. It is dosed 12.5-25 mg 1 hour before travel. Dimenhydrinate is indicated for adults and children two years and older; adult dosing: 50-100 mg every four to six hours PRN; dosing age two to five years: 12.5-25 mg every six to eight hours PRN; dosing age 6-12 years: 25-50 mg every six to eight hours.

A 35-year-old man presents to his PCP's office with a complaint of nausea. He has been experiencing abdominal discomfort and "queasiness" intermittently over the past couple of weeks. He has not taken any medication for this and simply lies down for a while until the nausea resolves. It is starting to impact his life enough that he now wants a medication to relieve the nausea and also to diagnose what is causing this problem. He has no significant past medical history. The patient denies black or tarry stools. The nausea is sometimes related to eating, but not always.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 160 lb Ht 69 in T 98.6°F BP 121/77 HR 76 RR 14 O_2 sat 99%

Physical exam reveals mild abdominal tenderness.

It appears the patient has a simple gastritis. Other testing will soon be done to formally diagnose the cause of the patient's nausea and abdominal discomfort. Today, a medication will be prescribed to help relieve his nausea.

Which of the following is the most appropriate prescription medication to use at this time?

A. dexamethasone
B. ondansetron
C. dronabinol
D. promethazine

Promethazine	Phenothiazines (promethazine, chlorpromazine, prochlorperazine)
Mechanism of Action	Anti emetic action comes from histamine 1 (H_1) antagonism
***Contraindications*/ Precautions**	*Hypersensitivity, coma, treatment of lower respiratory tract symptoms including asthma, age <2 years, intra-arterial or subcutaneous administration, avoid in Reye syndrome*/Serious tissue injury potential with injection, elderly (extrapyramidal and anticholinergic effects), bone marrow suppression, cardiovascular disease, glaucoma, myasthenia gravis, hepatic impairment, Parkinson disease, respiratory disease, seizures
Adverse Effects	Constipation, nausea, vomiting, dizziness, drowsiness, extrapyramidal symptoms, hypertension, hypotension, photosensitivity, thrombocytopenia, injection site reactions (mild to severe), blurred vision, respiratory depression
Drug Interactions	Ethanol, St. John's wort, sibutramine, metoclopramide, anticholinergics, inhibitors of CYP2B6 and 2D6, MAOIs, serotonin modulators, pramlintide
Monitoring	Mental status, injection site reaction (if IV), relief of symptoms
Case Notes	Phenothiazines are very useful for alleviating simple nausea and vomiting in adults with gastritis. In this case, an OTC item such as meclizine, an antacid, or H_2 antagonist may have also been appropriate. Dexamethasone is not appropriate for "simple" nausea due to unnecessary risks of adverse effects, but may be used in more severe cases. Ondansetron and dronabinol would also be reserved for more severe cases of nausea or prophylaxis. Oral antiemetic promethazine dosing: 12.5-25 mg every four to six hours as needed. Oral antiemetic chlorpromazine dosing: 10-25 mg every four to six hours as needed. Oral antiemetic prochlorperazine dosing: 5-10 mg three to four times daily; usual maximum: 40 mg/day.

A 56-year-old man was recently diagnosed with non-small cell lung cancer (NSCLC). He has smoked one to two packs of cigarettes a day since he was 15 years old. He is motivated to "beat cancer" so that he can be there for his grandchildren. He presents to the infusion center to receive chemotherapy treatment.

Allergies: NKDA

Medications: Gemcitabine 1,000 mg/m^2 IV on days 1, 8, and 15; cisplatin 100 mg/m^2 IV on day 1; repeat cycle every 28 days

Physical Exam/Other Studies:

Wt 170 lb Ht 70 in T 98.6°F BP 144/94 HR 84 RR 16 O_2 sat 98%

The patient's chemotherapeutic regimen carries a high risk of emesis, and he should, therefore, receive a combination antiemetic regimen consisting of three drugs. Two of these agents will be aprepitant and dexamethasone.

An additional agent from what drug class should be added to this antiemetic regimen?

5-HT_3 Receptor Antagonist	Ondansetron, dolasetron, granisetron, palonosetron
Mechanism of Action	Blocks serotonin peripherally at vagus nerve terminals and centrally in the chemoreceptor trigger zone
***Contraindications*/ Precautions**	*Hypersensitivity*/Those at risk for or taking medications that can cause QT prolongation; ileus or gastric distention
Adverse Effects	Headache, malaise/fatigue, constipation, drowsiness, dizziness, diarrhea, LFT elevation, QT interval prolongation, hypertension, bradycardia, tachycardia
Drug Interactions	Apomorphine, CYP3A4 inducers, rifamycin derivatives, QT-prolonging agents
Monitoring	LFTs, adverse effects, efficacy
Case Notes	Many chemotherapy treatments are known to induce nausea and emesis. The appropriate antiemetic regimen should be selected based on the expected risk of emesis of the chemotherapy. Chemotherapy regimens with a "high" emesis risk call for prophylaxis with a three-drug antiemetic regimen consisting of a 5-HT_3 receptor antagonist, a corticosteroid, and aprepitant. "Moderate" risk of emesis should be prophylaxed with a two-drug regimen of a 5-HT_3 receptor antagonist and a corticosteroid. There are many dosing options for oral and IV formulations, and choice may depend on the emetic risk of the chemotherapy regimen. Oral dosing is often adequate and should be given 30 minutes prior to chemotherapy. Dosing should be scheduled and not PRN.

A 56-year-old woman presents to your pharmacy with a prescription for an opioid to treat her chronic back pain. She had a motor vehicle accident approximately one week ago and will require surgery to reset her broken wrist. She tells you her pain ranks 9 on a scale of 1 to 10 every day. After seeing her physician and learning that it will be approximately two weeks before she can get her wrist surgery scheduled, she is prescribed a medication that should help get her through until the surgery. She is opioid naïve and inquires what side effects she should expect. She has approximately one panic attack every two weeks and does suffer from depression, but reports her medications are working well at this time.

Allergies: NKDA

Medications: Fluoxetine 40 mg capsule 1 po daily; alprazolam 1 mg tablet 1 po twice daily PRN

Physical Exam/Other Studies:

Wt 140 lb Ht 67 in

After filling her oxycodone extended-release 40 mg capsules and explaining that she is to take 1 po daily, you discuss with her the need for breakthrough pain coverage with her oxycodone 5 mg tablets, of which she was prescribed 1 po every four to six hours PRN breakthrough pain.

You also go over with her the potential side effects of opioid therapy, explaining to her that she could experience constipation. She does not want to suffer from this also, and asks if there is anything she can take to prevent this from occurring.

What medication would you recommend for this patient to prevent constipation while on opioid therapy?

Docusate	Emollient laxative (docusate sodium, docusate calcium, docusate potassium)
Mechanism of Action	Reduces surface tension of the oil-water interface of the stool, resulting in enhanced incorporation of water and fat allowing for stool softening
***Contraindications*/ Precautions**	*Hypersensitivity to docusate or any component of the formulation, concomitant use of mineral oil, intestinal obstruction, acute abdominal pain, nausea, or vomiting*/ Dependence, electrolyte imbalance with prolonged use
Adverse Effects	Intestinal obstruction, diarrhea, abdominal cramping, throat irritation
Drug Interactions	No significant drug interactions exist.
Monitoring	Improvement of constipation, adverse effects
Case Notes	Docusate is the best agent to prevent constipation in this patient. She will be on opiate therapy for a short period of time and therefore needs a way to prevent constipation. Recommend an increase in dietary fiber and water intake to help combat constipation. Docusate can be used in situations where it is helpful to avoid straining (eg, recovery from surgery, acute perianal disease, or rectal surgery). This agent will be most likely ineffective when used by chronic heavy opioid users or those with inadequate dietary fiber intake. Docusate is dosed orally 50-500 mg daily in one to four divided doses. Rectal administration is to add 50-100 mg docusate liquid to enema fluid and give as retention or flushing enema. Because the amount of sodium, calcium, or potassium is clinically insignificant, docusate salts are interchangeable.

A 79-year-old woman who lives in an assisted living center complains to you about her inability to pass stool. She states she has been constipated for approximately four days now and needs some relief for her condition. She says she usually does not drink more than one glass of water a day and does not eat the fruits or vegetables provided to her in her meals. She suffers from history of stroke, depression, hypertension, dyslipidemia, and Type 2 diabetes.

Allergies: Morphine (hives)

Medications: Clopidogrel 75 mg tablet 1 po daily; pravastatin 40 mg tablet 1 po every evening; citalopram 20 mg tablet 1 po daily; lisinopril 10 mg tablet 1 po twice daily; insulin glargine 25 units subcutaneously every evening; insulin aspart five units subcutaneously before every main meal

Physical Exam/Other Studies:

Wt 115 lb Ht 63 in T 98.5°F BP 118/68 HR 70 RR 18

Physical exam reveals abdominal bloating, distention, and tenderness.

Na 140 K 4.1 Cl 102 A1c 7.9% fasting glucose 128 SCr 1.2

You recommend she eat her vegetables and drink more water to help with her constipation. In the meantime, you need to recommend a therapy that will help regulate her stools again.

What class of medications for constipation would be the most appropriate first-line treatment for this patient?

Bulk-Forming Agents	Psyllium, methylcellulose, polycarbophil
Mechanism of Action	Bulk-forming agents absorb water in the intestine to form a viscous liquid that promotes peristalsis and reduces transit time.
***Contraindications*/ Precautions**	*Hypersensitivity to the individual agent or any component of the formulation; fecal impaction; GI obstruction*/ Coronary heart disease, GI disease, elderly; some dosage forms may contain calcium, phenylalanine, potassium, sodium, soy lecithin
Adverse Effects	Abdominal cramps, abdominal fullness, constipation, diarrhea, esophageal or bowel obstruction, bronchospasm
Drug Interactions	No significant drug interactions exist.
Monitoring	Resolution of constipation
Case Notes	Bulk-forming agents are the first-line treatment for geriatric patients or those in nursing homes. If one of these agents does not relieve this patient's constipation, more potent agents may be required. The doses to treat constipation are as follows: 2.5-30 g psyllium daily, 19 g methylcellulose up to three times daily, and 1.25 grams polycarbophil up to four times daily. Onset of action is 12-72 hours. The patient should drink at least eight ounces of water with each dose. Inadequate water intake may result in impaction, especially in the elderly. If impaction is noted, as it can occur with these agents, it must be removed via tap-water or saline enema or digital extraction before oral treatment can begin. Self-treatment of constipation should be limited to less than one week. If constipation persists, consult a healthcare provider. Bulk-forming agents like psyllium are soluble fibers. Insoluble fibers are also required in a patient's daily intake. Daily fiber requirements differ based on a person's gender and age. Ensure patients know their daily fiber requirement.

A 48-year-old woman presents to your pharmacy complaining of constipation. She has tried bulk-forming laxatives and complains that she keeps feeling more and more "full." She is looking for a way to relieve her constipation with something over-the-counter. Her past medical history consists of hysterectomy, HTN, osteopenia, and macular degeneration.

Allergies: NKDA

Medications: Lisinopril/hydrochlorothiazide 20/25 mg tablet 1 po every morning; calcium citrate/vitamin D 500 mg/200 IU tablet (OTC) 1 po twice daily; multivitamin with lutein tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 160 lb Ht 67 in

Physical exam deferred.

Lab values unavailable.

What class of over-the-counter laxatives is best for this patient in need of relief from constipation?

Stimulant Laxative	Bisacodyl, senna, magnesium sulfate
Mechanism of Action	Stimulates peristalsis by directly irritating the smooth muscle of the intestine, possibly the colonic intramural plexus; alters water and electrolyte secretion producing net intestinal fluid accumulation and laxation
***Contraindications/* Precautions**	*Hypersensitivity to the drug or a component of the formulation, abdominal pain or obstruction, nausea, or vomiting, intestinal inflammation, ulcerative colitis, appendicitis, pregnancy/* Self-medication in patients with constipation lasting longer than two weeks or in children less than two years of age
Adverse Effects	Electrolyte and fluid imbalance, mild abdominal cramping, nausea, rectal burning, vertigo, vomiting
Drug Interactions	Levels of bisacodyl may be decreased by antacids.
Monitoring	Resolution of constipation
Case Notes	A stimulant laxative will help the bowels to function properly again in this patient. She does not have a history of abusing laxatives and should be counseled on the proper use of stimulants. Senna dosing for adults with constipation is 15 mg po daily. Bisacodyl dosing for adults is 5-15 mg po as needed for complete evacuation. Administration on an empty stomach with a glass of water will provide most rapid results. Use of stimulant laxatives in the elderly population should be avoided. Senna can be used for bowel evacuation before a procedure. These medications should not be used routinely. The underlying cause of constipation should be identified and treated instead of long-term use of stimulant laxatives.

A 58-year-old man calls your pharmacy inquiring about a procedure he is getting ready to have at his physician's office. He says he is scheduled for a colonoscopy to determine if he has colon cancer or precancerous lesions, and he has been prescribed a medication he has never heard of and wants to know more information about it. He cannot remember the name of the medication but describes to you that it is supposed to clear out his bowels before the procedure begins.

Allergies: NKDA

Medications: Unknown

Physical Exam/Other Studies:
Not available

What medication is most commonly used for bowel evacuation before colonoscopy procedures?

Polyethylene Glycol Electrolyte Lavage Solution	Osmotic laxatives (glycerin, lactulose, polyethylene glycol 3350, polyethylene glycol electrolyte lavage solution, sorbitol)
Mechanism of Action	Induces catharsis by strong electrolyte and osmotic effects
***Contraindications*/ Precautions**	*Hypersensitivity to polyethylene glycol or any component of the formulation, ileus, GI obstruction, gastric retention, bowel perforation, toxic colitis, toxic megacolon*/Seizures, impaired gag reflex, ulcerative colitis
Adverse Effects	Malaise, abdominal distention, anal irritation, nausea, abdominal pain, vomiting, rigors, thirst, dizziness, headache, dyspepsia
Drug Interactions	No significant drug interactions exist.
Monitoring	Electrolytes, serum glucose, BUN, urine osmolality
Case Notes	Polyethylene glycol electrolyte lavage solution (PEG-ELS) is most commonly used for bowel evacuation before a colonoscopy or related procedure. Patients are instructed to not eat any solid foods two to three hours before beginning the PEG-ELS. Also, oral medications should be avoided for one hour before taking PEG-ELS. The patient should be instructed to take 240 mL (eight ounces) every 10 minutes until the four-liter bottle is consumed (maximum time, three hours) or the rectal effluent is clear and free of solid matter. Patients should expect the first bowel movement within one hour of beginning the administration process. Most formulations are dispensed with flavor packets to help improve palatability of the medication. Reconstituted solution should be refrigerated and must be used within 24-48 hours of preparation depending on specific product.

A 38-year-old woman presents to the clinic complaining of constipation that is unrelieved with all other products on the pharmacy shelves. She has tried emollients, stimulants, bulk-forming agents, and enemas, all with inconsistent results and minimal relief. She reports having a constant feeling of being full and having nausea. She is looking for something to help her treat her constipation. She has no past medical history besides chronic constipation.

Allergies: NKDA

Medications: Docusate 50 mg capsule (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 135 lb Ht 67 in BP 118/78 HR 80 RR 18

Physical exam reveals mild abdominal distention and tenderness.

Labs unavailable.

The physician diagnoses this patient with chronic idiopathic constipation and consults you for a therapeutic plan for her.

What medication is the best option to treat this patient's chronic idiopathic constipation?

Lubiprostone	Chloride channel activator
Mechanism of Action	Bicyclic fatty acid that acts locally at the apical portion of the intestine as a chloride channel activator, increasing intestinal fluid secretion and intestinal motility. Does not alter serum sodium or potassium concentrations.
***Contraindications*/ Precautions**	*Known or suspected mechanical bowel obstruction*/Dyspnea, nausea, diarrhea, GI obstruction, hepatic impairment, renal impairment; not approved for use in males or pediatrics
Adverse Effects	Headache, nausea, diarrhea, edema, chest discomfort, hypertension, dizziness, fatigue, insomnia, abdominal pain, flatulence, vomiting, loose stools, arthralgias, back pain, sinusitis, dyspnea, xerostomia
Drug Interactions	No significant drug interactions exist.
Monitoring	Resolution of constipation, adverse effects
Case Notes	Lubiprostone is the best choice for this patient because it is indicated for chronic idiopathic constipation. Adult dosing is 24 mcg po twice daily. If severe nausea occurs, dosing can decrease to 24 mcg po once daily. It should be taken with food and water to decrease nausea. It is also approved for females 18 and older with constipation-dependent IBS. Dosing for this diagnosis is 8 mcg po twice daily.

A 30-year-old man presents to the pharmacy with complaints of loose stools for the past 10 hours. He ate sushi for dinner last night at a restaurant that is known for not following proper health department standards. He started having episodes approximately two hours after dinner and they continued throughout the night. He describes his stools as having a watery consistency and says they occur approximately every 30 minutes.

Allergies: NKDA

Medications: Acetaminophen 325 mg tablet (OTC) 1-2 po every four to six hours PRN headache pain

Physical Exam/Other Studies:

Wt 156 lb Ht 70 in T 98.2°F BP 124/76 HR 86 RR 18

Physical exam reveals hyperperistalsis, borborygmi, and slight tenderness in the abdominal region.

This patient is looking for a recommendation of a medication to try over-the-counter for his diarrhea.

What medication would be the best recommendation for this patient?

Loperamide	Opiates and opioid derivatives (loperamide, diphenoxylate, difenoxin, paregoric)
Mechanism of Action	Acts through the opioid receptor in the intestinal muscles to inhibit peristalsis and prolong transit time; reduces fecal volume, increases viscosity, and diminishes fluid and electrolyte loss; demonstrates antisecretory activity; increases anal sphincter tone
***Contraindications*/ Precautions**	*Hypersensitivity to loperamide or any component of the formulation, abdominal pain without diarrhea, children <2 years, acute dysentery, acute ulcerative colitis, bacterial enterocolitis, pseudomembranous colitis*/Allergic reactions, discontinue if constipation, abdominal pain, or ileus develop, caution in patients with hepatic impairment, AIDS, caution in pediatrics
Adverse Effects	Dizziness, constipation, abdominal cramping, nausea, dry mouth, dyspepsia, flatulence
Drug Interactions	No significant drug interactions exist.
Monitoring	Episodes of diarrhea
Case Notes	Loperamide is the best OTC medication for this patient based on his symptoms and duration of diarrhea. Dosing instructions for acute diarrhea in an adult are 4 mg after the first loose stool and 2 mg after each additional loose stool, not to exceed 16 mg/day. Dosing for pediatric patients over the age of two is based on weight. In OTC labeling, if diarrhea lasts longer than two days, the patient should stop taking loperamide and consult a healthcare provider for further assistance and treatment. If a patient reports bloody diarrhea, the patient should not take loperamide and consult a healthcare provider. It is always important to remind a patient to stay hydrated during episodes of diarrhea. A combination product of loperamide and simethicone is available. Diphenoxylate is another common agent in this class available by prescription. It is formulated with a small amount of atropine to discourage abuse of the medication. Atropine can cause side effects of blurred vision, dry mouth, and urinary hesitancy. Difenoxin is also formulated with atropine. Paregoric is not widely used today because of abuse potential.

A 20-year-old woman presents to your pharmacy complaining of diarrhea. She states it started approximately one day ago and is so bothersome she had to miss all of her college classes today. She says she isn't sure what it could be, but did get home from Mexico late last night and thinks she may have caught something while she was there. After questioning a bit more, you find out she complains of nausea and indigestion as well as diarrhea. She is having a hard time eating anything, but has been drinking more fluids since her diarrhea started.

Allergies: Cephalosporins (rash)

Medications: Sumatriptan 50 mg tablet 1 po at onset of migraine; ibuprofen 200 mg tablet (OTC) 1 po every four to six hours PRN; multivitamin tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 110 lb Ht 62 in T 97.0°F BP 116/70 HR 16

What over-the-counter medication would you recommend for this patient to help treat all of her current symptoms?

Bismuth Subsalicylate	Antisecretory agent (bismuth subsalicylate, enzymes [lactase], bacterial replacement [*Lactobacillus acidophilus, Lactobacillus bulgaricus*])
Mechanism of Action	This product exhibits antisecretory, antimicrobial, and anti-inflammatory actions. The salicylate moiety is responsible for the antisecretory effects, and the bismuth exhibits antimicrobial action against bacterial and viral gastrointestinal pathogens.
***Contraindications*/ Precautions**	*Hypersensitivity to bismuth or any component of the formulation; do not use in children and teenagers with influenza or chickenpox because of risk of Reye's syndrome; hypersensitivity to salicylates; history of severe GI bleeding; history of coagulopathy; pregnancy (third trimester)*/Neurotoxicity, use with caution in children and patients taking aspirin
Adverse Effects	Anxiety, confusion, headache, mental depression, slurred speech, discoloration of the tongue, grayish black stools, impaction, muscle spasms, weakness, hearing loss, tinnitus
Drug Interactions	Bismuth may decrease the levels of tetracycline derivatives
Monitoring	Reduction in diarrhea, adverse reactions (tinnitus, impactions, CNS changes)
Case Notes	Bismuth subsalicylate is available over the counter and will help this patient with her current symptoms of diarrhea, nausea, and indigestion. This medication can also help with heartburn and dyspepsia as well. Patients should be assessed for aspirin allergies before taking this medication. Adult dosing is based on liquid containing 262 mg/15 mL or tablets containing 262 mg. Adults should take two tablets or 30 mL po every 30-60 minutes PRN up to eight doses in 24 hours. Dosing for pediatrics is based on age. Patients should be counseled on proper dosing due to salicylate toxicity risk. Patients suffering from *Helicobacter pylori* infections may be prescribed a combination regimen of bismuth subsalicylate plus antibiotics. Dosing for *H pylori* eradication is 524 mg four times daily with meals and at bedtime with combination therapy.

A 29-year-old woman presents to the clinic complaining of diarrhea. Her diarrhea comes and goes, but she can expect to experience approximately three to four episodes per week. She knows that lactose-containing foods aggravate her symptoms, so she knows to avoid them. She has tried controlling the diarrhea with over-the-counter lactose-digestion aids, but has been unsuccessful in finding one that works. For her diarrhea, she has tried controlling it with loperamide, but this therapy has failed and she is looking for other options today. She has no other conditions.

Allergies: NKDA

Medications: Loperamide 2 mg tablet (OTC) 2 po at onset of loose stool, 1 po each stool thereafter; multivitamin tablet (OTC) 1 po daily; acetaminophen 325 mg tablet (OTC) 1 po every four to six hours PRN

Physical Exam/Other Studies:

Wt 100 lb Ht 62 in BP 116/76 HR 66 RR 16

Physical exam reveals abdominal distention and borborygmi.

Labs unavailable at this time.

This patient is suffering from diarrhea-predominant irritable bowel syndrome (IBS). The physician approaches you for a recommendation of a medication that can help her.

What medication is the best option for this patient's diarrhea-predominant IBS?

Alosetron	Selective 5-HT_3 receptor antagonist (alosetron, dolasetron, granisetron, ondansetron, palonosetron)
Mechanism of Action	Alosetron selectively antagonizes serotonin 5-HT_3 receptors, or ligand-gated ion channels, in the GI tract as well as other peripheral and central locations.
***Contraindications*/ Precautions**	*Constipation, hypersensitivity to alosetron or any component of the formulation, history of severe or chronic constipation or sequelae from constipation, ischemic colitis, intestinal obstruction, stricture, toxic megacolon, gastrointestinal perforation and/or adhesions, diverticulitis, Crohn disease, ulcerative colitis, hepatic impairment, impaired intestinal circulation, thrombophlebitis, hypercoagulable state*/Appropriate use, constipation, ischemic colitis, hepatic impairment, patients must read and sign the patient-physician agreement before receiving their first prescription
Adverse Effects	Constipation, abdominal discomfort/pain, nausea, abdominal distention, hemorrhoids, regurgitation and reflux
Drug Interactions	Substrate of CYP1A2 (major); avoid use with apomorphine, fluvoxamine (increased effect/toxicity); decreased effect of alosetron seen with rifamycin derivatives
Monitoring	Symptoms of IBS, diarrhea, constipation
Case Notes	Because this patient has failed traditional therapy with loperamide and continues to have symptoms from her IBS, alosetron is the best option. Discontinue this medication immediately if constipation develops. Only physicians enrolled in a special prescribing program may prescribe this medication for their patients due to potential serious gastrointestinal side effects. An FDA-approved patient medication guide must be dispensed with this prescription for each prescription and refill. Efficacy of this medication has only been established in females. Other agents in this class are approved for treatment of chemotherapy-induced nausea and vomiting.

A 35-year-old man presents to the emergency room complaining of uncontrollable watery diarrhea and severe flushing of the face and neck. After tests are run, the team of physicians you are working with identifies that he has what is called "carcinoid syndrome," a condition that occurs when a patient has a tumor that secretes vasoactive substances such as histamine, bradykinin, serotonin, and prostaglandins. His past medical history consists of hypertension, asthma, hypoglycemia, and perennial allergic rhinitis.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; fluticasone/salmeterol 500/50 mcg inhaler 1 inhalation po twice daily; albuterol HFA inhaler 1-2 puffs po every four to six hours PRN; loratadine 10 mg tablet (OTC) 1 po daily; ibuprofen 200 mg tablet (OTC) 1-2 po every four to six hours PRN

Physical Exam/Other Studies:

Wt 167 lb Ht 69 in T 96.9°F BP 129/82 HR 86 RR 16

Physical exam reveals no significant findings.

Na 137 K 3.9 Cl 100 glucose 109 SCr 0.8

As the physicians determine if the tumor is operable, they look to you to identify what medication can help with this man's symptoms.

What medication is the best choice to help control this patient's secretory diarrhea?

Octreotide	Somatostatin analog (octreotide, lanreotide, vapreotide)
Mechanism of Action	Mimics natural somatostatin by inhibiting serotonin release and the secretion of gastrin, VIP, insulin, glucagon, secretin, motilin, and pancreatic polypeptide.
***Contraindications*/ Precautions**	*Hypersensitivity to octreotide or a component of the formulation*/Chronic treatment is associated with an abnormal Schilling's test, impaired gallbladder function, suppression of TSH secretion, alterations in dietary fats, and increased toxicity of other QTc-prolonging agents; be cautious in patients with CVD, diabetes, excessive fluid loss, hepatic/renal impairment
Adverse Effects	Sinus bradycardia, chest pain, fatigue, headache, malaise, fever, dizziness, pruritus, hyperglycemia, abdominal pain, loose stools, nausea, diarrhea, cholelithiasis
Drug Interactions	Avoid use with artemether, dronedarone, lumefantrine, nilotinib, pimozide, quinine, tetrabenazine, thioridazine, ziprasidone; see drug monograph for complete listing of interactions.
Monitoring	Evaluate therapeutic effectiveness according to use and adverse effects (blood glucose, thyroid, cardiovascular changes, GI disturbances, CNS changes, and dyspnea).
Case Notes	In a patient who is not a candidate for surgery of the offending tumor, watery diarrhea is managed by octreotide. Octreotide is proven effective for the treatment of chemotherapy-induced diarrhea as well as carcinoid tumors, other peptide-secreting tumors, and dumping syndrome. Symptoms of carcinoid syndrome include flushing of the face and neck and severe, watery diarrhea stimulated by an emotional outbreak or by ingestion of food or drinking alcohol. Dosage for adults with diarrhea is 50-100 mcg IV every eight hours, increasing by 100 mcg/dose at 48-hour intervals, to a maximum dose of 500 mcg every eight hours. Patients with diabetes should monitor their blood sugars closely when on this medication due to the risk of hyperglycemia. In addition to secretory diarrhea, octreotide is used to treat acromegaly, bleeding esophageal varices, Cushing syndrome, small bowel fistulas, and pancreatic tumors, among other conditions.

A 28-year-old woman presents to her PCP's office to discuss treatment of her ulcerative colitis (UC). She has no other significant past medical history. She had been taking sulfasalazine to maintain remission of her UC, but stopped it two weeks ago due to intolerable stomach upset and nausea clearly associated with the medication. These symptoms have since resolved. She is now having UC symptoms of mild abdominal cramping and bloody diarrhea (two to three small-volume stools per day). She has no other complaints.

Allergies: NKDA

Medications: Sulfasalazine 500 mg tablet 2 po twice daily (held for two weeks); ethinyl estradiol/drospirenone 0.02 mg/3 mg tablets 1 po daily for birth control

Physical Exam/Other Studies:

Wt 134 lb Ht 64 in T 98.6°F BP 118/74 HR 84 RR 12 O_2 sat 99%

Physical exam reveals mild abdominal tenderness.

Elective sigmoidoscopy revealed erythematous intestinal mucosa with shallow, continuous ulcerations in the rectum and distal colon.

Her UC is classified as mild. Sulfasalazine is stopped to avoid adverse effects, and a new medication needs to be started to regain and maintain remission.

Which of the following therapeutic options is most appropriate?

A. oral mesalamine derivative
B. mesalamine suppository
C. oral prednisone
D. IV hydrocortisone

Mesalamine (5-ASA) Derivative (oral)	Various brands differ by release mechanism
Mechanism of Action	Specific mechanism of action is unknown; it is thought to modulate local chemical mediators of the inflammatory response topically, or to inhibit tumor necrosis factor (TNF).
***Contraindications*/ Precautions**	*Hypersensitivity to mesalamine, aminosalicylates, or salicylates*/Hepatic impairment, renal impairment, peptic ulcer, pyloric stenosis, elderly
Adverse Effects	Headache, pain, abdominal pain, diarrhea, constipation, eructation, nausea, pharyngitis, chest pain, edema, reduced Clcr, reduced hemoglobin/hematocrit
Drug Interactions	Antacids, H_2 antagonists, proton pump inhibitors, cardiac glycosides, heparin, low molecular weight heparin, thiopurine analogues, varicella vaccine
Monitoring	CBC and renal function
Case Notes	Mesalamine derivatives are appropriate for inducing and maintaining remission of mild UC. The mesalamine suppository is only appropriate for lesions isolated to the rectum (proctitis). The mesalamine enema would also be appropriate because this is mild disease of the rectum and effects may not reach the distal colon. Prednisone is for treatment of moderate UC and is not used for maintenance. IV hydrocortisone is for treatment of severe disease. Tablets or capsules should be taken with meals and swallowed whole (do not break, crush, or chew). Dosing varies among agents and depends on the indication: treatment of active disease or maintaining remission. Products differ by the mechanism of release of the drug. Different products release medication to different locations within the small intestine and/or colon. Products are selected based on location of lesions in the GI tract or on subtle differences in adverse effect profiles.

A 26-year-old woman presents to her family physician's office for an exacerbation of her Crohn disease (CD). Her symptoms have included a week of abdominal pain, fevers to 101°F, and intermittent diarrhea that progressed to six bowel movements per day despite her typically effective high doses of oral mesalamine.

Allergies: NKDA

Medications: Mesalamine controlled-release 500 mg capsule 2 po four times daily

Physical Exam/Other Studies:

Wt 128 lb Ht 66 in T 101.7°F BP 138/92 HR 90 RR 15 O_2 sat 99%

Physical exam reveals mild abdominal pain without rebound tenderness.

Previously performed colonoscopy revealed CD lesions located in the terminal ileum and colon.

Her CD exacerbation is classified as moderate.

What is the best choice for management (at this point in time)?

A. prednisone
B. sulfasalazine
C. azathioprine
D. mesalamine enema

Prednisone	Systemic corticosteroid (prednisone, budesonide, prednisolone, methylprednisolone, dexamethasone, cortisone, hydrocortisone)
Mechanism of Action	Decreases neutrophil migration and reverses capillary permeability to prevent or control inflammation
***Contraindications*/ Precautions**	*Serious infections (except septic shock or tuberculosis), systemic fungal infections, varicella infections, administration with live or live, attenuated vaccines*/Patients with hyperglycemia, tuberculosis, untreated systemic infections, thyroid dysfunction, hypertension, osteoporosis, thromboembolic tendency, peptic ulcer
Adverse Effects	Effects seen with short- or long-term use include edema, hypertension, psychoses, insomnia, headache, impaired wound healing, bruising, hyperglycemia, weight gain, increased appetite, nausea, vomiting, muscle weakness, and immunosuppression. Effects seen primarily with long-term or frequent use include HPA suppression, Cushing syndrome, growth suppression, peptic ulcer, decreased bone mineral density, fractures, cataracts, and glaucoma.
Drug Interactions	CYP3A4 substrate and inducer. Levels may increase in the presence of a CYP3A4 inhibitor, increasing the rate of adverse effects.
Monitoring	Blood pressure, weight, glucose
Case Notes	Oral steroids like prednisone are appropriate for gaining control of moderate active CD. Once control is gained, attempts should be made to taper off of steroids and maintain remission with other agents. Sulfasalazine would not be any more effective in this case than the mesalamine already being used. Topical mesalamine enema would not be effective due to the location of the lesions as well as the current failure of oral mesalamine. Azathioprine may be used to gain control or maintain remission, but may take months to become effective. This makes azathioprine an appropriate add-on agent after oral steroids have reduced severity of disease.

A 34-year-old woman presents to her PCP's office for a follow-up visit for her ulcerative colitis (UC). In recent history, it was necessary to add high-dose prednisone to her treatment regimen of high-dose sulfasalazine to successfully control her UC symptoms. As her PCP attempted to wean her off of the prednisone, her symptoms recurred, and the prednisone dose had to be increased again to regain control with multiple attempts. Her UC is currently "steroid-dependent."

Allergies: NKDA

Medications: Sulfasalazine 500 mg tablet 2 po four times daily; prednisone 20 mg tablet 3 po daily

Physical Exam/Other Studies:

Wt 130 lb Ht 67 in T 98.6°F BP 122/78 HR 78 RR 14 O_2 sat 99%

Physical exam reveals no pertinent findings.

Her UC is currently stable and she is asymptomatic while on the medications listed above.

What is the best choice for management (at this point in time)?

A. stop the oral prednisone
B. stop the oral prednisone and switch to intravenous hydrocortisone
C. add azathioprine
D. continue current medications since symptoms are controlled

Azathioprine	Immunosuppressant (mercaptopurine)
Mechanism of Action	Suppresses the immune system by antagonizing purine metabolism and may inhibit synthesis of DNA, RNA, and proteins; may also interfere with cellular metabolism and inhibit mitosis
***Contraindications*/ Precautions**	*Hypersensitivity, pregnancy, patients with rheumatoid arthritis treated with alkylating agents*/Should be prescribed by physicians familiar with the risks, including hematologic toxicities and mutagenic potential; chronic immunosuppression increases the risk of neoplasia; thiopurine methyltransferase (TPMT) deficiency, hepatic impairment, renal impairment, infection
Adverse Effects	Nausea, vomiting, diarrhea, leukopenia, thrombocytopenia, hepatotoxicity, infection, myalgia
Drug Interactions	Numerous specific interactions. Please refer to product labeling for complete list of interactions.
Monitoring	For use as immunomodulatory therapy in CD or UC, monitor CBC with differential weekly for one month, then biweekly for one month, followed by monitoring every one to two months throughout the course of therapy. LFTs should be assessed every three months.
Case Notes	Oral steroids like prednisone are appropriate for moderate to severe UC. Once controlled, attempts should be made to taper off of steroids and maintain remission with other agents and to avoid undesirable adverse effects of long-term steroid use; attempts should be made to reduce the dose and ultimately wean from prednisone. Chronically used prednisone cannot be stopped abruptly without a taper. IV hydrocortisone is not appropriate in this case and is used for severe exacerbations. Azathioprine may be used to gain control or maintain remission, but may take months to become effective. This makes azathioprine an appropriate add-on agent in steroid-dependent cases and may allow a successful steroid taper. Dosing for reduction of steroid use in CD or UC: 50 mg once daily; may increase by 25 mg/day every one to two weeks as tolerated to target dose of 2-3 mg/kg/day; adjust dose with renal impairment or TPMT deficiency. Azathioprine is also used for rheumatoid arthritis and organ transplants.

A 27-year-old woman returns to her PCP for a follow-up visit about her Crohn disease (CD). She has struggled to gain control of her CD despite treatments with mesalamine, prednisone, and mercaptopurine. She was recently diagnosed with enterocutaneous fistulas as a complication of her CD. This has become a significant disturbance in her life in addition to her refractory CD, and she would like another treatment that may assist her overall condition.

Allergies: NKDA

Medications: Mesalamine controlled-release 500 mg capsule 2 po four times daily; prednisone 20 mg tablet 1 po daily; mercaptopurine 50 mg tablet 2 po daily

Physical Exam/Other Studies:

Wt 142 lb Ht 68 in T 98.6°F BP 126/82 HR 84 RR 14 O_2 sat 99%

Physical exam reveals evidence of perianal fistulas.

Which of the following drugs may be added to this patient's regimen to assist the healing of enterocutaneous fistulas?

A. olsalazine
B. cyclosporine
C. methotrexate
D. infliximab

Infliximab	TNF blocker/biologic (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab)
Mechanism of Action	Infliximab is a chimeric monoclonal antibody that binds to human tumor necrosis factor alpha (TNFα), inhibiting its activity. This may reduce induction of proinflammatory cytokines, reduce neutrophil activity, and reduce leukocyte migration.
***Contraindications*/ Precautions**	*Hypersensitivity to infliximab or murine proteins; doses >5 mg/kg in patients with moderate or severe heart failure (NYHA Class III/IV)*/ Autoimmune, hematologic, or seizure disorders, hepatitis B, infections, malignancies, tuberculosis (TB), demyelinating CNS disease, heart failure
Adverse Effects	Nausea, diarrhea, abdominal pain, dyspepsia, headache, URI, infusion reaction, infection, hypertension, fatigue, fever, rash, increased LFT, anemia, leukopenia, neutropenia, fracture, arthralgia
Drug Interactions	Abatacept, abciximab, anakinra, canakinumab, certolizumab pegol, denosumab, leflunomide, natalizumab, pimecrolimus, rilonacept, sipuleucel-T, trastuzumab, vaccines
Monitoring	Infusion reactions, signs of infection, LFT, place and read PPD prior to starting therapy
Case Notes	Infliximab is the only option in this question indicated to treat enterocutaneous fistulas in CD. Cyclosporine's role is in severe, refractory CD as an option to colectomy. Methotrexate and olsalazine are not indicated for fistula treatment. Dosing regimen for treatment of CD: 5 mg/kg at zero, two, and six weeks, followed by 5 mg/kg every eight weeks; dose may be increased to 10 mg/kg in patients who respond but then lose their response. Infuse over at least two hours; do not infuse with other agents; antihistamines, acetaminophen, and corticosteroids may be used to manage infusion reactions along with a decrease in infusion rate. If no response by week 14, consider discontinuing therapy. Immunizations must be current prior to administration; TB skin tests (PPD) should be performed prior to and during therapy, and latent TB should be treated prior to administering infliximab; avoid live vaccines concurrently.

A 52-year-old man is brought to the hospital emergency room by his wife with a two-day history of cognitive impairment and "confusion." His past medical history is significant for liver cirrhosis (three years) and Type 2 diabetes. In the past, he has experienced ascites and portal hypertension, but his cirrhosis has been relatively stable over the past year. Yesterday, he became very confused and unable to perform routine tasks around the house. Today, his confusion persists and he has been making inappropriate statements about his surroundings. He is disoriented to time and place. His wife explains that he was fine at his PCP visit two weeks ago. At that visit, they even spoke with a diabetes educator, and for the past week have significantly changed his diet in an effort to better control his blood glucose. He replaced most of his carbohydrate intake with beef and other protein. No other changes were made.

Allergies: NKDA

Medications: Propranolol 20 mg tablet 1 po twice daily; insulin glargine 22 units subcutaneously daily

Physical Exam/Other Studies:

Wt 202 lb Ht 70 in T 98.6°F BP 114/72 HR 78 RR 16 O_2 sat 99%

Physical exam reveals a man in no acute distress who is disoriented to time and place; trace lower extremity edema bilaterally.

AST 70 ALT 58 Alk Phos 160 T bili 1.6 Alb 3.0 INR 1.4 NH_3 152

A1c 7.5 Glu 205 SCr 1.0 K 4.1 Na 134

The patient is diagnosed with hepatic encephalopathy likely as a result of his recent excessive dietary intake of protein. Among other things, his hyperammonemia must be addressed.

What medication should be given to specifically treat his hepatic encephalopathy?

Lactulose	Ammonium detoxicant; osmotic laxative
Mechanism of Action	Degradation of lactulose by bowel flora leads to an acidic colonic pH; this causes ammonia (NH_3) to convert to ammonium (NH_4), which is eliminated in stool.
***Contraindications*/ Precautions**	*Hypersensitivity, galactosemia*/Caution in diabetes as product contains galactose and lactose; electrolyte imbalance
Adverse Effects	Diarrhea, nausea, vomiting, abdominal discomfort, cramping, flatulence
Drug Interactions	None
Monitoring	Serum potassium, serum ammonia, fluid status
Case Notes	Lactulose is standard therapy for acute or chronic hepatic encephalopathy to reduce hyperammonemia. Neomycin and metronidazole may be used as treatments if lactulose fails, but are not used first-line due to risk of toxicity. The patient's sudden diet change to low-carbohydrate and high-protein intake likely caused his encephalopathy. His diet should be protein restricted to help correct the encephalopathy and prevent future episodes. Need for other supportive measures to manage his underlying liver failure should be assessed. Oral dosing: 45 mL every one to two hours until catharsis, then may reduce to 15-45 mg (to produce two to three soft stools daily) every 8-12 hours. Rectal retention enema dosing: 300 mL diluted in 1 L of water or normal saline and retained for 30-60 minutes every four to six hours. Available as a solution for home use. Neomycin has a different mechanism, but may also be used for hepatic encephalopathy; neomycin dose is 500-2,000 mg every six to eight hours or 4-12 g/day divided every four to six hours for five to six days. Rifaximin also has a different mechanism, but may be used for reduction of overt hepatic encephalopathy recurrence; rifaximin dose is 550 mg twice daily.

A 42-year-old woman returns to her PCP to discuss treatment options for her gallstones. Her past medical history is significant for obesity. She has tried many fad diets in the past to lose weight. Her most recent attempt resulted in a rapid loss of 32 pounds. Shortly following this rapid weight loss, she started experiencing sharp right upper quadrant pain episodically that would last for 5-15 minutes at a time. Her PCP had said that her rapid weight loss likely caused her to develop gallstones. Imaging studies from last week confirm the diagnosis of gallstones without obstructions. The patient adamantly refuses surgery to remove the stones, but wants a treatment.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 212 lb Ht 67 in T 98.6°F BP 126/84 HR 86 RR 12 O_2 sat 99%

Physical exam reveals an obese female in no acute distress.

Imaging shows stones <20 mm in diameter.

Due to the nature of the likely etiology of her gallstones, the stones are likely cholesterol stones and not calcified. The stones are noted to be small in size.

What medication could be given to the patient to help dissolve her gallstones?

Ursodiol	Cholelitholytic
Mechanism of Action	Reduces cholesterol secretion from the liver and reabsorption from the intestines; this decreases the cholesterol content in the bile and bile stones
***Contraindications*/ Precautions**	*Hypersensitivity, allergy to bile acids; not for use with calcified-cholesterol, radiopaque, or bile pigment stones; patients with unremitting acute cholecystitis, cholangitis, biliary obstruction, gallstone pancreatitis, or biliary-gastrointestinal fistula*/Caution in hepatic impairment or with a nonvisualizing gallbladder; confirm appropriate use
Adverse Effects	Headache, dizziness, diarrhea, constipation, dyspepsia, nausea, vomiting, back pain, upper respiratory infection, alopecia, rash, flatulence, urinary tract infection, cholecystitis, arthralgia, myalgia, increased serum creatinine, cough, pharyngitis
Drug Interactions	Aluminum hydroxide, bile acid sequestrants, fibric acid derivatives, estrogens
Monitoring	LFTs
Case Notes	Ursodiol is indicated for dissolution of gallstones in patients with radiolucent, noncalcified gallbladder stones <20 mm in greatest diameter who are not candidates for cholecystectomy because of systemic disease, advanced age, idiosyncratic reaction to general anesthesia, or refusal of surgery and is considered the pharmacologic treatment of choice in these patients. Dissolution usually requires several months of therapy and complete dissolution may not occur; recurrence is reported in up to 50% of patients. Monitor for recurrence of stones. May be used in obese patients who are rapidly losing weight to prevent gallstones. Available as a 300 mg capsule or 250 or 500 mg tablet (tablet indicated for primary biliary cirrhosis). Oral treatment dose: 8-10 mg/kg/day in two to three divided doses; use beyond 24 months is not established. Oral prevention dose: 300 mg capsule twice daily.

A 34-year-old woman presents to her PCP's office to discuss travel to a foreign country. She is participating in a medical mission trip in six months to a country considered to have an intermediate to high endemicity of hepatitis A virus (HAV). She has no significant past medical history. She believes she will likely be in direct contact with people infected with HAV. Her vaccination history is incomplete. She doubts she has had all routine vaccinations.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 128 lb Ht 65 in T 98.6°F BP 118/74 HR 80 RR 12 O_2 sat 99%

Physical exam reveals a healthy female in no acute distress.

Negative titers reveal a need for several vaccines.

At a minimum, what vaccine should be included in her upcoming set of immunizations?

Hepatitis A Vaccine	Inactive viral vaccine
Mechanism of Action	Provides active immunization against HAV infection at an effective immune response rate
***Contraindications*/ Precautions**	*Hypersensitivity*/Anaphylactic reactions can occur; caution with acute illness, bleeding disorders, active hepatitis A infection, immunocompromised patients
Adverse Effects	Irritability, drowsiness, headache, fever; injection site pain, warmth, swelling, erythema; rash menstrual disorder, anorexia, nausea, vomiting, diarrhea, myalgia, back pain, muscle stiffness, cough, upper respiratory infection, pharyngitis
Drug Interactions	Immunosuppressants
Monitoring	LFTs
Case Notes	The Advisory Committee on Immunization Practices (ACIP) recommends routine hepatitis A vaccination for: all children ≥12 months of age; travelers to countries with intermediate to high endemicity of HAV; persons who anticipate close personal contact with an international adoptee from a country of intermediate to high endemicity of HAV during their first 60 days of arrival into the United States (eg, household contacts, babysitters); men who have sex with men; illegal drug users; patients with chronic liver disease; patients who receive clotting-factor concentrates; or persons who work with HAV-infected primates or with HAV in a research laboratory setting. IM doses vary for adults versus children; see dosing for the two individual brand products. When used for primary immunization, the vaccine should be given at least two weeks prior to expected HAV exposure. When used prior to an international adoption, the vaccination series should begin when adoption is being planned, but ideally ≥2 weeks prior to expected arrival of adoptee.

A 38-year-old man presents to his PCP's office after returning from international travel. The man returned to the United States four days ago. Yesterday, he learned that there has been an outbreak of hepatitis A virus (HAV) in the region overseas where he has spent the past two weeks. Because it was not an area with intermediate or high endemicity of HAV, he did not receive the HAV vaccine prior to his trip. He has no significant past medical history. The man is concerned about contracting HAV and would like to explore post exposure prophylaxis.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 152 lb Ht 67 in T 98.6°F BP 132/76 HR 75 RR 12 O_2 sat 99%

Physical exam reveals an asymptomatic male in no acute distress.

What can be given to this patient for post exposure prophylaxis of hepatitis A virus?

Immune Globulin (Ig)	Immune globulin; blood product derivative
Mechanism of Action	Provides passive immunity by increasing the antibody titer and antigen-antibody reaction potential
***Contraindications*/ Precautions**	*Hypersensitivity, IgA deficiency, severe thrombocytopenia or coagulation disorders where IM injections are contraindicated*/Anaphylactic reactions can occur; because this is a human blood product, there is risk of infectious agents that could cause disease.
Adverse Effects	Flushing, angioedema, chills, lethargy, fever, urticaria, erythema, nausea, vomiting, local irritation or muscle stiffness, myalgia
Drug Interactions	Live vaccines
Monitoring	None
Case Notes	Ig may be used for pre- or postexposure prophylaxis of HAV. Ig provides protection by passive transfer of antibody and is most effective if given in the incubation period of infection; use within the first two weeks reduces infectivity in 85% of patients. Ig is indicated for: Hepatitis A: Within 14 days of exposure and prior to manifestation of disease; Measles: For use within six days of exposure in an unvaccinated person, who has not previously had measles; Varicella: When varicella zoster immune globulin is not available; Rubella: Postexposure prophylaxis (within 72 hours) to reduce the risk of infection in exposed pregnant women who will not consider therapeutic abortion; Immunoglobulin deficiency: To help prevent serious infections. IM dosing for HAV: Pre-exposure prophylaxis upon travel into endemic areas (hepatitis A vaccine preferred): 0.02 mL/kg for anticipated risk of exposure <3 months; 0.06 mL/kg for anticipated risk of exposure ≥3 months; repeat dose every five months if exposure continues. Postexposure prophylaxis: 0.02 mL/kg given within 14 days of exposure; Ig is not needed if at least one dose of hepatitis A vaccine was given at ≥1 month before exposure.

A 20-year-old pharmacy student presents to the campus student clinic to complete his required immunizations. He has received the complete vaccines for tetanus, diphtheria, pertussis, varicella zoster, measles, mumps, rubella, and annual influenza. He has no significant past medical history.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 150 lb Ht 67 in T 98.6°F BP 112/74 HR 74 RR 12

Physical exam was not performed.

What vaccine series does he still need to receive?

Hepatitis B Vaccine	Inactivated vaccine
Mechanism of Action	Confers active immunity via formation of anti-hepatitis B antibodies
***Contraindications*/ Precautions**	*Hypersensitivity to yeast, hepatitis B vaccine, or any component of the formulation*/Anaphylactic reaction may occur; use caution in acute illness, active hepatitis B, cardiopulmonary disease, multiple sclerosis, immunocompromised, and elderly patients
Adverse Effects	Injection site reactions, flushing, hypotension, agitation, dizziness, fatigue, chills, fever, rash, insomnia, headache, angioedema, urticaria, abdominal pain, nausea, vomiting, diarrhea, constipation, loss of appetite, dysuria, myalgia, arthralgia, back pain, stiff neck, cough, ear ache, pharyngitis, upper respiratory tract infection, flu-like syndrome
Drug Interactions	Immunosuppressants
Monitoring	Adverse reactions
Case Notes	Healthcare professionals including students should receive the three-dose series of hepatitis B vaccine. Regimen consists of three doses (zero, one, and six months) given IM. Vaccinate persons with any of the following indications and any person seeking protection from hepatitis B virus (HBV) infection: Behavioral: sexually active persons who are not in a long-term, mutually monogamous relationship; persons seeking evaluation or treatment for a sexually transmitted disease; current or recent injection-drug users; and men who have sex with men; Occupational: healthcare personnel and public-safety workers who are exposed to blood or other potentially infectious body fluids; Medical: persons with end-stage renal disease, including patients receiving hemodialysis; persons with HIV infection; and persons with chronic liver disease; Other: household contacts and sex partners of persons with chronic HBV infection; clients and staff members of institutions for persons with developmental disabilities; and international travelers to countries with high or intermediate prevalence of chronic HBV infection.

A 36-year-old woman presents to her gastroenterologist's office to discuss her recent lab results for her chronic hepatitis B virus (HBV). Her past medical history is significant for hypertension and HBV without cirrhosis. She has no complaints and denies any symptoms of disease.

Allergies: NKDA

Medications: Hydrochlorothiazide 12.5 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 144 lb Ht 67 in T 98.6°F BP 116/84 HR 82 RR 14

Physical exam reveals a female in no acute distress.

AST 104 ALT 162

HBsAg (+) HBeAg (+) HBV DNA >20,000 IU/mL

What first-line agent can be used to treat her chronic hepatitis B virus with the least likelihood of resistance?

Pegylated Interferon Alfa-2a (INF)	Interferon (pegylated interferon alfa-2a, pegylated interferon alfa-2b [different indication])
Mechanism of Action	Alpha interferons are a family of proteins, produced by nucleated cells that have antiviral, antiproliferative, and immune-regulating activity.
***Contraindications*/ Precautions**	*Hypersensitivity; autoimmune hepatitis; decompensated liver disease in cirrhotic patients (Child-Pugh score >6); decompensated liver disease (Child-Pugh score ≥6, class B and C) in chronic hepatitis C co-infected with HIV; neonates and infants*/Autoimmune disease, concomitant use with ribavirin, infectious disorders, ischemic disorders, neuropsychiatric disorders, pregnancy, diabetes, thyroid disorders, anemia, renal impairment
Adverse Effects	Headache, fatigue, pyrexia, dermatitis, nausea, vomiting, anorexia, diarrhea, weight loss, abdominal pain, neutropenia, anemia, increased ALT, injection site reaction, muscle weakness, myalgia, arthralgia, dyspnea, hyper/hypothyroid
Drug Interactions	Aldesleukin, methadone, ribavirin, telbivudine, zidovudine, theophylline
Monitoring	CBC (including hemoglobin, WBC, and platelets) and chemistries (including liver function tests and uric acid) measured at weeks one, two, four, six, and eight, and then every four to six weeks (more frequently if abnormal); TSH measured every 12 weeks
Case Notes	First-line treatment of HBV can be with INF, entecavir, or tenofovir. INF is not associated with resistance, but nucleoside or nucleotide analogues (lamivudine, adefovir, entecavir, telbivudine, and tenofovir) may promote resistance. Entecavir and tenofovir cause less resistance than the others and may be considered first-line options with INF in terms of efficacy. In HBeAg-positive patients, treatment should be started when the ALT is elevated and HBV DNA count is >20,000 IU/mL. Subcutaneous dose of INF for chronic hepatitis B: 180 mg once weekly for 48 weeks.

A 15-year-old female patient presents to the physician with a chief complaint of fatigue. She has noticed over the last six months that she feels like she is always tired. She sleeps 8-10 hours each night, often falls asleep at school, and takes a nap when she gets home from school in the afternoon. She is a basketball player and has noticed that she does not have as much endurance as before. She is developing normally and started menses at 14 years of age. She has no known medical conditions and is on no medications.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 115 lb Ht 63 in T 98.9°F BP 112/71 HR 98 RR 12 O_2 sat 100%

Physical exam reveals a pale appearance

Na 131 K 3.5 Cl 99 CO_2 27 fasting glucose 95 BUN 16 SCr 0.7

TSH 7 T_4 6

Hgb 10.4 (12-15.2) Hct 34 (36-47) RBC 5 (4.5-5.1) MCV 68 (78-96) Platelets 270 (150-450) Serum ferritin 6 (7-140)

Based on the laboratory parameters above, what medication would you recommend for this patient to help with her fatigue?

Iron Supplement	Ferrous sulfate, ferrous gluconate, ferrous fumarate, carbonyl iron
Mechanism of Action	Replenishes depleted iron stores in the bone marrow
***Contraindications*/ Precautions**	*Hemochromatosis, hemolytic anemia, hypersensitivity to iron*/Peptic ulcer, enteritis, ulcerative colitis
Adverse Effects	Gastrointestinal irritation, epigastric pain, constipation, diarrhea, dark stools, discoloration of the urine, liquid preparations may stain teeth temporarily
Drug Interactions	Iron absorption may be decreased with antacids and tetracyclines. Iron may decrease the absorption of tetracyclines, levothyroxine, methyldopa, levodopa, and fluoroquinolones.
Monitoring	Hemoglobin, ferritin, iron, total iron binding capacity, reticulocyte count
Case Notes	This patient has iron deficiency anemia as evidenced by the low hemoglobin, MCV, and ferritin. Recent onset of menses may have put the patient at risk for iron deficiency. The ferrous sulfate salt form is best absorbed. A typical starting dose would be 200 mg of elemental iron daily in two divided doses. Once-daily administration will work but will take longer to achieve benefit. Ideally, iron products will be given one hour before meals. If the patient does not tolerate this due to GI side effects, iron can be administered with meals, but absorption will be reduced by more than half. Administration with at least 200 mg vitamin C per 30 mg elemental iron increases iron absorption. Increasing meat and orange juice intake with meals will assist with iron absorption. Milk and tea should be minimized between meals as they will decrease iron absorption. Treatment should be continued for three to four months after the hemoglobin and hematocrit return to normal to replenish body stores.

A 72-year-old woman presents to the physician with a chief complaint of tingling in her fingers and around her mouth. She has noticed these sensations for several months but she feels they have increased over the past couple of months. Her past medical history is significant for gastroesophageal reflux and hypertension.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po once daily; omeprazole 20 mg capsule 1 po once daily

Physical Exam/Other Studies:

Wt 124 lb Ht 67 in T 98.9°F BP 132/81 HR 62 RR 13 O_2 sat 100%

Physical exam reveals glossitis

Hgb 11.3 (12-16) Hct 33 (36-46) MCV 132 (80-100) Serum ferritin 83 (12-150) vitamin B_{12} 94 (100-900) folate 10 (1.8-16)

Based on the laboratory parameters above, what medication would you recommend for this patient to help with her neuropathy?

Vitamin B_{12} (cyanocobalamin)	Cyanocobalamin tablet, lozenge, intranasal solution, sublingual tablet, injection solution
Mechanism of Action	Coenzyme for fat and carbohydrate metabolism and protein synthesis, and used for hematopoiesis
***Contraindications*/ Precautions**	*Hereditary optic nerve atrophy, hypersensitivity to cyanocobalamin or cobalt*/Impaired renal function
Adverse Effects	Hypokalemia, thrombocytosis
Drug Interactions	Cyanocobalamin absorption is decreased by colchicines, extended-release potassium, aminosalicylic acid, omeprazole, alcohol, phenytoin, and phenobarbital. Large doses of vitamin C will degrade cyanocobalamin.
Monitoring	Potassium during initiation of therapy, hemoglobin, hematocrit, reticulocyte count, platelets, serum cyanocobalamin and folate, methylmalonate, total homocysteine
Case Notes	This patient has vitamin B_{12} deficiency anemia as evidenced by low hemoglobin, high MCV, and low B_{12}. The aging population is at high risk for deficiency due to atrophic gastritis, malabsorption of vitamin B_{12}, and frequent use of acid suppressants. This patient's neurologic manifestations will hopefully reverse but can be permanent if the deficiency has been present for a prolonged period of time. Due to the very low serum level and neurologic manifestations, therapy should be started with deep subcutaneous injections at 1,000 mcg cyanocobalamin daily for one week, followed by weekly injections for one month, and then monthly. Parenteral therapy can be used if more rapid resolution is desired. Improvement in glossitis is expected within 24 hours, and hemoglobin begins to rise in the first week. A CBC and B_{12} level is recommended after one to two months and then every three to six months. Patients should be educated to increase dietary intake of fortified cereals, meat, fish, poultry, and dairy products.

A 16-year-old male patient presents to the hospital for acute chest syndrome secondary to sickle cell anemia. This is his second episode of acute chest syndrome in two years. He also has a history of six to eight hospitalizations per year for pain crises. He currently receives blood transfusions every three weeks. Past medical history is significant for hypertension

Allergies: Sulfamethoxazole/trimethoprim (rash)

Medications: Lisinopril 20 mg tablet 1 po once daily; folic acid 1 mg tablet 1 po once daily; deferasirox 500 mg tablet 3 po once daily

Physical Exam/Other Studies:

Wt 162 lb Ht 68 in T 100.6°F BP 142/91 HR 110 RR 22

The patient is in significant pain and distress.

The medical team is working to stabilize the patient and control his pain. One of the medical residents would like to know if there is something else that can be done to decrease the incidence of his vaso-occlusive crises.

What medication could be used to decrease the frequency of vaso-occlusive crises in this patient?

Hydroxyurea	Antineoplastic
Mechanism of Action	For sickle cell anemia, hydroxyurea increases fetal hemoglobin levels by stimulating the production of fetal hemoglobin. Fetal hemoglobin is less likely to sickle. It also increases nitric oxide levels, decreases neutrophils and monocytes, and decreases red blood cell adhesion to the endothelium. As an antineoplastic, it inhibits DNA synthesis during the S-phase of cell division.
Contraindications/ **Precautions**	*Severe anemia (Hgb <4.5) or bone marrow suppression (neutrophils <2,000 or platelets <80,000), pregnancy (category D), hypersensitivity*/Renal impairment, prior radiotherapy or chemotherapy
Adverse Effects	Bone marrow suppression, headache, malaise, hair loss, nail changes, nausea, hepatotoxicity, peripheral neuropathy, renal tubular function impairment, secondary leukemia (long-term use)
Drug Interactions	Avoid use with natalizumab or live vaccines. Hydroxyurea levels may be increased by didanosine or trastuzumab and decreased by echinacea.
Monitoring	CBC every two weeks during titration and every four to six weeks thereafter. Serum creatinine, liver function tests, serum uric acid, fetal hemoglobin
Case Notes	Because this patient has had an episode of acute chest syndrome and ≥3 pain crises in a year, he is a candidate for hydroxyurea. Hydroxyurea has been shown to decrease the frequency of painful episodes of acute chest syndrome, blood transfusions, and hospitalizations. Although it is only FDA approved in adults for this indication, studies in children and adolescents have proven benefit and hydroxyurea is recommended in this population. The recommended dose is 10-15 mg/kg/day, increased by 5 mg/kg/day after 8-12 weeks if tolerated. The maximum recommended daily dose is 35 mg/kg/day. It typically takes three to six months before an improvement is seen. Treatment should be temporarily discontinued if the neutrophil count is <2,000; platelet count is <80,000; hemoglobin is <5; serum creatinine increases by 50%, or LFTs increase by 100%.

A 32-year-old woman presents to the hematology clinic for routine evaluation of sickle cell anemia. She has been receiving blood transfusions every four weeks for a little over a year and has seen a dramatic decrease in pain crises.

Allergies: NKDA

Medications: Lisinopril 20 mg tablet 1 po once daily; folic acid 1 mg tablet 1 po once daily; lansoprazole 30 mg capsule 1 po once daily

Physical Exam/Other Studies:

Wt 184 lb Ht 65 in BP 124/81 HR 82 RR 14

Her labs reveal a serum ferritin of 2,500 ng/mL, which is elevated.

What type of medication could be used to decrease this patient's serum ferritin?

Iron Chelating Agents	Deferoxamine (IM, IV, SQ), deferasirox (PO)
Mechanism of Action	Deferoxamine complexes with ferric ions to form ferrioxamine, which is removed by the kidneys. Deferasirox binds iron, forming a complex that is excreted through the feces.
***Contraindications/* Precautions**	*Severe renal disease, hemochromatosis, hypersensitivity*/Hepatic impairment, pre-existing hematologic disorders
Adverse Effects	Both agents can cause ocular and otic toxicity, rash, and gastrointestinal discomfort. Deferoxamine may cause flushing and hypotension when given IV and may impair cardiac function. Deferasirox may cause impairment of renal function and hepatitis.
Drug Interactions	Deferoxamine may be increased by ascorbic acid. Deferasirox may decrease levels of CYP3A4 substrates. Deferasirox may be decreased by aluminum hydroxide.
Monitoring	Serum creatinine, CBC, LFT, serum ferritin, annual auditory and ophthalmic exam
Case Notes	The risk for iron overload is high after one year of chronic transfusions, and iron chelation therapy is recommended when serum ferritin is greater than 1,500-2,000 ng/mL. The oral dosage form of deferasirox is convenient, but adherence and adverse effects can limit its use. The recommended dose for deferasirox is 20 mg/kg/day, increased by 5-10 mg/kg/day every three to six months up to 30 mg/kg/day. Deferoxamine, when used for chronic iron overload, can be given IV or by subcutaneous infusion via a portable pump. The IV dose is 15 mg/kg/hour up to 6 grams/day at a rate no more than 15 mg/kg/hour, and subcutaneous dose is 1-2 g/day over 8-24 hours. Deferoxamine may also be used for acute iron intoxication and aluminum-induced bone disease in chronic renal failure.

A 10-year-old girl is in the clinic to follow-up from an outpatient course of chemotherapy for acute lymphocytic leukemia. She is currently in the consolidation phase of treatment. Her only complaint at this visit is that she is fatigued. She tolerated her last chemotherapy with minimal nausea. She has not yet started menses.

Allergies: NKDA

Medications: Mercaptopurine 50 mg tablet 1 po on Monday, Wednesday, Friday, and Sunday and one-and-a-half tablets on Tuesday, Thursday, and Saturday; cyclophosphamide 1,000 mg IV push given five days ago; cytarabine 75 mg IV push given for four days, last dose yesterday; methotrexate 12 mg intrathecal, given yesterday; sulfamethoxazole/trimethoprim 800/160 mg tablet, 1 po on Friday, Saturday, and Sunday; ondansetron 4 mg tablet, 1 po as needed for nausea

Physical Exam/Other Studies:

Wt 62 lb Ht 52 in BP 90/61 HR 84 RR 14

Physical exam reveals no pertinent findings.

Urinalysis: SG 1.020 pH 7.8 Blood 4+ Protein 4+ WBC 0-5 cells/hpf LE neg Nitrite neg

Chemistry: Na 126 K 3.5 Cl 110 CO_2 18 BUN 18 SCr 1.8 Glucose 94

She is diagnosed with hemorrhagic cystitis. Which of her medications is responsible for this adverse effect?

Cyclophosphamide	Antineoplastic, alkylating agent, nitrogen mustard (cyclophosphamide, ifosfamide)
Mechanism of Action	Alkylation and cross-linking DNA strands, inhibiting DNA replication
***Contraindications/* Precautions**	*Hypersensitivity*/Bone marrow suppression, impaired renal or hepatic function
Adverse Effects	Alopecia, hyponatremia, nausea, vomiting, mucositis, hemorrhagic cystitis, nephrotoxicity, hepatotoxicity, sterility, secondary tumors
Drug Interactions	CYP2B6 and 3A4 substrate, CYP3A4 inhibitor
Monitoring	CBC, urinalysis, serum electrolytes, serum creatinine, urine specific gravity, urine output
Case Notes	Hemorrhagic cystitis occurs in 5-10% of patients receiving cyclophosphamide and is due to toxic effects of the metabolite acrolein on the bladder. It typically is detected by routine urinalysis. If blood is visible in the urine, the cystitis is considered serious and can lead to death. Treatment is limited to aggressive hydration. Prevention is crucial and is achieved by providing twice maintenance fluids before and after infusion and ensuring the urine specific gravity is ≤1.010 before administration. Mesna is routinely given with cyclophosphamide doses greater than 1 g/m^2 and any dose of ifosfamide to prevent hemorrhagic cystitis. This patient is receiving 1 g/m^2 and would not routinely receive mesna; however, it would now be recommended that she receive mesna with any future doses of cyclophosphamide due to this complication. Cyclophosphamide and all alkylating agents are known to cause decreased or absent fertility and have been associated with secondary cancers. Cyclophosphamide's emetogenic potential depends on the dose, with doses <750 mg/m^2 considered as having moderate, doses of 750-1,500 mg/m^2 considered as having moderately high, and doses ≥1,500 mg/m^2 considered as having high emetogenic potential. Ifosfamide has moderate emetogenic potential that does not vary with the dose. Other non-nitrogen mustard alkylating agents include: carmustine (bischloroethylnitrosurea), lomustine, procarbazine, dacarbazine, and temozolomide.

A 24-year-old man is in the hospital for chemotherapy. He has Hodgkin's lymphoma and is completing his third cycle of chemotherapy. He has tolerated chemotherapy well up to this point with the exception of nausea.

Allergies: NKDA

Medications: Doxorubicin 25 mg/m^2 IV; bleomycin 10 mg/m^2 IV; vinblastine 6 mg/m^2 IV; dacarbazine 375 mg/m^2 IV

Physical Exam/Other Studies:

Wt 192 lb Ht 70 in BP 128/81 HR 68 RR 12

Physical exam reveals no pertinent findings.

Echo: pending

Chest x-ray: pending

The orders state to wait until the echocardiogram results have returned to mix his chemotherapy. Which of his antineoplastic agents has the potential to cause abnormal echocardiogram findings?

Doxorubicin	Antineoplastic agent, anthracycline (doxorubicin, daunorubicin, epirubicin, idarubicin)
Mechanism of Action	Inhibit topoisomerase II, leading to double-strand DNA breaks and intercalating DNA
***Contraindications/* Precautions**	*Severe CHF, cardiomyopathy, myelosuppression, previous treatment with anthracycline derivatives, cardiac irradiation, or cumulative dose 550 mg/m*^{2}/Impaired hepatic function
Adverse Effects	Cardiomyopathy, arrhythmias, infertility, stomatitis, nausea, vomiting, diarrhea, red/orange discoloration of the urine, myelosuppression, elevation of liver enzymes
Drug Interactions	Substrate of CYP2D6 and 3A4. Inhibitor of CYP2B6, 2D6, 3A4. Avoid use with natalizumab and live vaccines.
Monitoring	CBC, echocardiogram, LFT, IV site for extravasation
Case Notes	Cardiac toxicity with anthracyclines may be acute (arrhythmias) or chronic (CHF), and each dose should not be given until confirmation that the patient's echocardiogram is normal. The cardiac toxicity is a result of free radical damage to the cardiac muscle. The onset of CHF may develop years after completion of chemotherapy. Chronic cardiac toxicity is associated with cumulative doses of any anthracycline to which the patient has been exposed in their lifetime. Therefore, the cumulative dose of each agent factors into the recommended maximum lifetime dose. When calculating the patient's BSA, the IBW should be used. Dose should be adjusted for a bilirubin >1. Myelosuppression onset is seven days with nadir at 10-14 days and recovery at 21-28 days.

A 40-year-old woman is admitted to the hospital for chemotherapy for acute lymphocytic leukemia. She is currently in the consolidation phase of treatment. She has had difficulty tolerating previous courses of chemotherapy due to delayed nausea and vomiting. Her chemotherapy will consist of cyclophosphamide 1,500 mg/m^2 and cytarabine 75 mg/m^2. She has received 24 hours of hydration with twice usual maintenance fluids.

Allergies: NKDA

Medications: Mercaptopurine 50 mg tablet 1 po on Monday, Wednesday, Friday, and Sunday and one-and-a-half tablets on Tuesday, Thursday, and Saturday; sulfamethoxazole/trimethoprim 800/160 mg tablet 1 po on Friday, Saturday, and Sunday

Physical Exam/Other Studies:

Wt 124 lb Ht 65 in BP 127/74 HR 74 RR 18

Physical exam reveals no pertinent findings.

Urinalysis: SG 1.008 pH 6.8 Blood neg Protein neg

Chemistry: Na 131 K 3.8 Cl 110 CO_2 21 BUN 20 SCr 1.1 Glucose 82 AST 24 ALT 35 Direct Bilirubin 0.4

CBC: WBC 2.1 Segs 52% Bands 4% Lymphs 40% Monos 4% Hgb 10.1

This is a highly emetogenic chemotherapy regimen. The physician has written a prescription for granisetron 100 mg and dexamethasone 12 mg by mouth prior to chemotherapy. What additional medication would you recommend for prophylaxis of acute nausea and vomiting?

Aprepitant	Antiemetic, substance P/neurokinin 1 receptor antagonist (aprepitant, fosaprepitant)
Mechanism of Action	Substance P interacts with the neurokinin 1 receptor to cause both acute and delayed nausea and vomiting. Aprepitant is an antagonist of substance P/neurokinin 1 receptors.
***Contraindications/* Precautions**	*Hypersensitivity, concurrent use with pimozide, astemizole, or cisapride*/Severe hepatic insufficiency
Adverse Effects	Hypotension, bradycardia, flushing, dehydration, fatigue, headache, insomnia, anxiety, constipation, heartburn, hiccups, weakness, proteinuria
Drug Interactions	Moderate CYP3A4 inhibitor and substrate. Avoid use with cisapride, everolimus, pimozide, and tolvaptan.
Monitoring	Fatigue, weakness, signs and symptoms of dehydration
Case Notes	The cyclophosphamide dose places it in the high emetogenic category, and cytarabine at this dose would have low emetogenicity. The American Society of Clinical Oncology recommends the use of a serotonin reuptake inhibitor (dolasetron, granisetron, or ondansetron), dexamethasone, and aprepitant for regimens with high emetic risk and for regimens containing an anthracycline and cyclophosphamide. The recommended dose is 125 mg by mouth one hour before chemotherapy followed by 80 mg on days two and three after chemotherapy. For patients who need an intravenous option, fosaprepitant may be used at a dose of 115 mg 30 minutes prior to chemotherapy followed by oral aprepitant on days two and three. Dexamethasone is also recommended for days two and three after chemotherapy at a dose of 8 mg.

A 72-year-old man presents to the clinic complaining of ringing in his ears for the past two weeks. He is receiving chemotherapy for stage III non-small cell lung cancer, including cisplatin and paclitaxel every 21 days. He has received six cycles. His past medical history is also significant for hypertension and hyperlipidemia.

Allergies: NKDA

Medications: Lisinopril 10 mg/hydrochlorothiazide 12.5 mg tablet 1 po daily; atorvastatin 40 mg tablet 1 po daily; cisplatin 75 mg/m^2 IV every 21 days; paclitaxel 175 mg/m^2 IV every 21 days; ondansetron 8 mg tablet 1 po every eight hours PRN nausea or vomiting

Physical Exam/Other Studies:
Wt 132 lb Ht 68 in BP 131/78 HR 82 RR 15
Physical exam reveals no pertinent findings.
Audiogram: High-frequency hearing loss

Which of this patient's medications is likely causing his high-frequency hearing loss?

Cisplatin	Antineoplastic agent, alkylating agent, platinum derivative (cisplatin, carboplatin, oxaliplatin)
Mechanism of Action	Platinum binding to DNA leading to intrastrand and interstrand DNA cross-links
Contraindications/ **Precautions**	*Renal impairment, hearing impairment, myelosuppression, pregnancy, hypersensitivity/* Ensure adequate hydration and magnesium levels before starting
Adverse Effects	Highly emetogenic, hypomagnesemia, myelosuppression, nephrotoxicity, anaphylaxis, peripheral neuropathy, high-frequency hearing loss
Drug Interactions	Avoid using with natalizumab and live vaccines. Cisplatin may increase levels of aminoglycosides, taxane derivatives, topotecan, vinorelbine, and natalizumab. Cisplatin may be increased by trastuzumab and decreased by echinacea.
Monitoring	Renal function, electrolytes, audiogram, LFT, CBC, urine output, nausea
Case Notes	The platinum derivatives can cause high-frequency hearing loss that can progress to complete hearing loss. The risk is increased with total cumulative doses of >400 mg/m^2. This patient has received 450 mg/m^2. Cisplatin and carboplatin are considered the backbone of lung cancer chemotherapy. In most cases, doses should not exceed 120 mg/m^2 per treatment course. Dose adjust for any Clcr ≤50 mL/minute. Onset of myelosuppression is 10 days with a nadir at 18-23 days and recovery at 21-40 days. Peripheral neuropathy is more likely to occur with cumulative doses >200 mg/m^2.

A 67-year-old man is completing his first cycle of chemotherapy for non-Hodgkin's lymphoma. He has tolerated the medications well and is preparing to go home.

Allergies: NKDA

Medications: Cyclophosphamide 750 mg/m^2 IV one dose given two days ago; doxorubicin 50 mg/m^2 IV one dose given two days ago; vincristine 2 mg IV one dose given two days ago; prednisone 50 mg tablet 1 po once a day started two days ago and has three doses left; aprepitant 80 mg tablet 1 po yesterday and today, 125 mg tablet given two days ago

Physical Exam/Other Studies:

Wt 210 lb Ht 72 in BP 132/81 HR 71

Physical exam reveals no pertinent findings.

This regimen is associated with a high risk of prolonged neutropenia and neutropenic fever. What class of medications is recommended to decrease neutropenic complications with this regimen?

Colony-Stimulating Factors	Filgrastim (granulocyte colony-stimulating factor [G-CSF]), sargramostim (granulocyte-macrophage colony-stimulating factor [GM-CSF]), pegfilgrastim (pegylated G-CSF)
Mechanism of Action	G-CSF stimulates the production, maturation, and activation of neutrophils. GM-CSF stimulates the production and activity of neutrophils, eosinophils, monocytes, and macrophages.
Contraindications/ Precautions	*Hypersensitivity to colony-stimulating factors, allergy to yeast (GM-CSF), allergy to* E coli *proteins (G-CSF), ≥10% myeloid blasts in bone marrow or peripheral blood, history of idiopathic thrombocytopenia purpura (GM-CSF)*/Do not give within 24 hours of chemotherapy, pre-existing cardiac conditions, gout, psoriasis, renal or hepatic impairment
Adverse Effects	Chest pain, exacerbation of skin disorders, leukocytosis, elevated LFTs, bone pain
Drug Interactions	Filgrastim may increase the levels of topotecan
Monitoring	CBC, renal function, liver function
Case Notes	The American Society of Clinical Oncology recommends the use of colony-stimulating factors for the prevention of neutropenic fever with regimens that place patients at a ≥20% risk of febrile neutropenia such as the CHOP regimen this patient is receiving. This patient's age (>65 years) also places him at high risk for infections. In high-risk circumstances, colony-stimulating agents are recommended to be used with antibiotics during an episode of neutropenic fever. The recommended dose of filgrastim is 5 mcg/kg/day starting 24-72 hours after completing chemotherapy. It should be continued until the patient's ANC is 2-3 × 10^9/L. GM-CSF is licensed specifically for bone marrow transplant and AML and would typically not be used in patients with lymphoma. Pegfilgrastim can be given once after each course of chemotherapy rather than daily, but has not been thoroughly studied in this population for safety and efficacy.

A 72-year-old man presents to the clinic to begin treatment for prostate cancer. During a routine digital rectal exam three weeks ago, a large prostate was discovered. A PSA level was then drawn, and a biopsy revealed localized prostate cancer. His primary complaint at this time is impotence. His past medical history is significant for hypertension and hyperlipidemia

Allergies: NKDA

Medications: Hydrochlorothiazide 12.5 mg tablet 1 po once daily; atorvastatin 40 mg tablet 1 po once daily; aspirin 81 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 184 lb Ht 74 in BP 124/78 HR 62 RR 13

Physical exam reveals no pertinent findings.

PSA: 24 ng/mL

Free PSA: 7%

Which of the following drug treatments is considered first choice for treatment of prostate cancer?

A. 5 α-reductase inhibitor

B. luteinizing hormone-releasing hormone agonist

C. antiandrogen

D. chemotherapy

Luteinizing Hormone-Releasing Hormone Agonist (LHRH agonists)	Leuprolide, leuprolide depot, leuprolide implant, triptorelin depot, triptorelin implant, goserelin acetate implant
Mechanism of Action	Reduce testosterone secretion by the testes and causing pituitary receptor downregulation
***Contraindications*/ Precautions**	*Hypersensitivity*/Cardiovascular disease, psychiatric illness
Adverse Effects	Tumor flare with worsening symptoms during first two weeks (ureteral or bladder outlet obstruction, bone pain), edema, headache, depression, insomnia, fatigue, dizziness, hyperlipidemia, decreased libido, nausea/vomiting, injection site reaction, nervousness, angina, decreased bone density
Drug Interactions	Decreased effectiveness of antidiabetic agents
Monitoring	LH, FSH, and testosterone two to four weeks after initiation of therapy; bone mineral density, PSA, paresthesias, blood sugar, lipids
Case Notes	LHRH agonists are currently considered first-line therapy due to a decreased rate of cardiovascular events compared to estrogen and prolonged survival compared to antiandrogens. Leuprolide is given subcutaneously once daily, while depot formulations are given IM or subcutaneously every one, three, or four months depending on the formulation chosen. Leuprolide implants deliver 12 months of therapy. Triptorelin is given IM every one, three, or six months. Goserelin is given subcutaneously every one to three months. Efficacy is thought to be similar for each agent; thus the choice is typically made based on patient preference and cost. Patients should be counseled on the occurrence of a disease flare during the first two weeks of therapy, which may manifest as hot flashes, erectile dysfunction, bone pain, or urinary symptoms. This will typically resolve within two weeks. Treating prostate cancer should result in resolution of this patient's sexual dysfunction.

A 39-year-old woman presents to the women's health clinic to begin therapy for breast cancer. She has been diagnosed with a low-risk, stage II breast cancer that is hormone receptor positive. She has completed radiation therapy as well as surgical resection. She has no other significant past medical history and is premenopausal.

Allergies: Penicillin (rash)

Medications: Multivitamin tablet 1 po daily

Physical Exam/Other Studies:

Wt 142 lb Ht 66 in BP 126/74 HR 71 RR 12

Physical exam reveals no pertinent findings.

The physician plans to start adjuvant endocrine therapy to decrease the risk for relapse.

What endocrine therapy is preferred for use in this patient?

Tamoxifen	Antineoplastic agent, selective estrogen receptor modulator (tamoxifen, toremifene)
Mechanism of Action	Binds to estrogen receptors producing a complex that decreases DNA synthesis and inhibits estrogen effects. Cytostatic.
***Contraindications/* Precautions**	*Hypersensitivity; if using for cancer prevention, history of DVT or PE is a contraindication/* Thromboembolic events
Adverse Effects	Flushing, hypertension, peripheral edema, mood changes, hot flashes, vaginal discharge, weight loss, weakness, arthralgia, bone marrow suppression, hepatotoxicity, ocular abnormalities, thromboembolic events, decreased bone mineral density
Drug Interactions	CYP2D6, 2C9, and 3A4 substrate; inhibitor of 2C8 and P-glycoprotein; grapefruit juice may decrease tamoxifen metabolism; avoid black cohosh, dong quai, St. John's wort
Monitoring	CBC, calcium, LFTs, cholesterol, signs/symptoms of DVT or PE, bone mineral density, ophthalmic exams
Case Notes	For premenopausal, hormone receptor-positive, low-risk patients, tamoxifen is the recommended therapy. Alternatively, LHRH agonists or ovarian ablation may be utilized. The recommended dose is 20 mg once daily for five years. For those that are intermediate or high risk, chemotherapy is given before starting tamoxifen. Toremifene is currently only indicated for the treatment of metastatic disease. Raloxifene is also a selective estrogen receptor modulator, but it has not been shown to be beneficial in the treatment of breast cancer, and its use is limited to the treatment and prevention of osteoporosis.

A 43-year-old woman is admitted to the hospital for chemotherapy. She has ovarian cancer and is completing her second cycle of chemotherapy. She is showing signs of peripheral neuropathy as manifested by numbness in her hands and feet, which has been improving over the past week.

Allergies: NKDA

Medications: Paclitaxel 175 mg/m^2 IV as a three-hour infusion; carboplatin 520 mg IV; methylprednisolone 125 mg IV 30 minutes before chemotherapy; diphenhydramine 50 mg IV 30 minutes before chemotherapy; ranitidine 50 mg IV 30 minutes before chemotherapy

Physical Exam/Other Studies:

Wt 124 lb Ht 65 in BP 118/71 HR 81 RR 12

Physical exam reveals no pertinent findings.

Which of her antineoplastic agents requires pretreatment with methylprednisolone, diphenhydramine, and ranitidine to reduce her risk for fatal hypersensitivity?

Paclitaxel	Antineoplastic agent, antimicrotubular (docetaxel, paclitaxel)
Mechanism of Action	Promotes the assembly of microtubules and prevents depolymerization. Blocks cells in the late G2 phase and M phase of the cell cycle.
***Contraindications/* Precautions**	*Hypersensitivity*/Peripheral neuropathy, hepatic impairment, severe neutropenia
Adverse Effects	Hypotension or hypertension, arrhythmias, ataxia, confusion, myelosuppression, elevated transaminases, peripheral neuropathy, diplopia, anaphylaxis
Drug Interactions	Substrate of CYP2C8 and 3A4. Avoid use with natalizumab and live vaccines.
Monitoring	CBC, ECG, LFT, injection site, BP, HR
Case Notes	There is a 2-4% risk of anaphylaxis with paclitaxel administration that may be fatal. Therefore, pretreatment 30-60 minutes before infusion is necessary. Fatal reactions can still occur with premedication. Epinephrine, fluids, diphenhydramine, and steroids should be available at the bedside in the event of a reaction. Because this patient has peripheral neuropathy, a dose reduction may be necessary to prevent progression to severe neuropathy. Dosage adjustments are also recommended if the bilirubin or AST is elevated.

A 64-year-old man is admitted to the hospital to begin chemotherapy. He has been diagnosed with metastatic colorectal cancer and has undergone surgical resection.

Allergies: NKDA

Medications: Morphine sulfate 20 mg extended-release capsule 1 po every eight hours; morphine sulfate 10 mg immediate-release tablet 1 po every four hours PRN; irinotecan 180 mg/m^2 IV every two weeks; leucovorin 400 mg/m^2 IV every two weeks; fluorouracil 400 mg/m^2 IV on day one then 1,200 mg/m^2/day for two days every two weeks

Physical Exam/Other Studies:

Wt 140 lb Ht 67 in BP 124/76 HR 74 RR 13

Physical exam reveals no pertinent findings.

Which of this patient's medications is a topoisomerase inhibitor?

Irinotecan	Antineoplastic agent, topoisomerase I inhibitor (irinotecan, topotecan)
Mechanism of Action	Binds to topoisomerase I-DNA resulting in double-strand DNA breakage and cell death
***Contraindications*/ Precautions**	*Concurrent use with St John's wort or ketoconazole, severe bone marrow failure, hypersensitivity*/Elevated total bilirubin (>2 mg/dL), impaired renal function
Adverse Effects	Diarrhea, neutropenia, nausea and vomiting, asthenia, abdominal pain, alopecia, cholinergic symptoms, elevated transaminases, elevated bilirubin
Drug Interactions	Substrate of CYP2B6 and 3A4. Avoid use with atazanavir, natalizumab, St. John's wort, live vaccines.
Monitoring	Electrolytes, renal function, CBC, LFT, bilirubin, diarrhea
Case Notes	Dose-limiting adverse effects include diarrhea and myelosuppression. Diarrhea may be early onset (two to six hours) or late onset (1-12 days). Early-onset diarrhea may be treated with atropine, while late-onset diarrhea is treated with loperamide regularly at the first sign of soft stools. Single doses should not exceed 700 mg. Patients should be treated with a 5-HT_3 antagonist and dexamethasone 30 minutes prior to administration.

A 53-year-old man presents for evaluation to the liver transplant clinic. His past medical history includes end-stage liver disease secondary to hepatitis C infection. His past medical history includes end-stage liver disease secondary to hepatitis C infection, jaundice, kidney dysfunction, pruritus, and gout.

Allergies: NKDA

Medications: Furosemide 20 mg tablet 1 po twice daily; allopurinol 100 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 175 lb Ht 69 in T 97.1°F BP 123/79 HR 58 RR 16 O_2 sat 98%

Physical exam and laboratory values are not yet known.

Prior to his appointment, you meet with the transplant physician to plan for this patient's possible liver transplant and to design his immunosuppression regimen.

In addition to prednisone and cyclosporine, what immunosuppression medication will this patient need following his transplant?

Mycophenolate Mofetil	Antimetabolite (azathioprine, mycophenolate mofetil, mycophenolic acid)
Mechanism of Action	Mycophenolate inhibits inosine monophosphate dehydrogenase, which inhibits guanosine nucleotide synthesis resulting in decreased proliferation of T and B lymphocytes.
***Contraindications/* Precautions**	Contraindications and precautions are listed for mycophenolate; please refer to azathioprine product information for specifics regarding that agent. *Hypersensitivity to the agent or any component of the formulation/*Limit use to experienced physicians; may cause infection, lymphoproliferative disorders, avoid use in pregnancy, may cause latent viral infections, neutropenia, pure red cell aplasia, avoid use in patients with hypoxanthine-guanine phosphoribosyltransferase deficiency, peptic ulcer disease, renal impairment
Adverse Effects	Diarrhea, nausea, leukopenia, thrombocytopenia
Drug Interactions	Food delays the absorption of mycophenolate; avoid antacids and cholestyramine, which both decrease the AUC; cyclosporine may decrease mycophenolate levels
Monitoring	CBC, renal and liver function, signs/symptoms of infection, pregnancy test
Case Notes	Antimetabolite agents are typically included in the immunosuppressive regimen for most types of solid organ transplants. The use of azathioprine has declined due to its higher rate of adverse reactions and toxicities. Additionally, this patient is on allopurinol for gout, and allopurinol can inhibit xanthine oxidase, increasing the bioavailability of azathioprine fourfold. Therefore, mycophenolate would be preferred in this patient. Patients will often complain of gastrointestinal side effects with mycophenolate. To combat this, smaller doses may be given more frequently or at a lower dose. If the WBC decreases below 3×10^3 cells/mm^3 or if the ANC is less than $1.3 \times 10^3/\mu L$, mycophenolate should be reduced or discontinued. The usual dose in adults is between 500-2,000 mg/day.

A 59-year-old woman presents to the transplant clinic for a routine follow-up visit. She had a kidney transplant five years ago secondary to uncontrolled hypertension.

Allergies: NKDA

Medications: Modified cyclosporine 100 mg capsule 3 po twice daily; mycophenolate mofetil 500 mg tablet 2 po twice daily; prednisone 5 mg tablet 1 po once daily; famotidine 20 mg tablet 1 po twice daily; calcium citrate 500 mg/vitamin D 200 IU tablet (OTC) 1 po twice daily; amlodipine 10 mg tablet 1 po once daily; metoprolol 25 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 155 lb Ht 64 in T 97.3°F BP 128/75 HR 60 RR 18 O_2 sat 98%

Physical exam is unremarkable.

SCr 0.8 TC 240 LDL 138 HDL 39 TG 212

Cyclosporine trough 248 ng/mL

Which of her medications is most likely contributing to her dyslipidemia?

Cyclosporine	Calcineurin inhibitor (cyclosporine, tacrolimus)
Mechanism of Action	Inhibits the production of IL-2 and other cytokines by T cells, leading to blocked T-cell proliferation through inhibition of calcineurin phosphatase activity
***Contraindications/* Precautions**	*Hypersensitivity to cyclosporine; when using in rheumatoid arthritis or psoriasis: abnormal renal function, uncontrolled hypertension, malignancies, concomitant use with PUVA or UVB therapy, methotrexate, other immunosuppressive agents, coal tar, or radiation/*For use only by an experienced physician, infection, hypertension, nephrotoxicity, skin cancer, do not interchange products, malignancy, hepatotoxicity, reduce dose when used with everolimus, transplant patients, live vaccines
Adverse Effects	Hyperlipidemia, nephrotoxicity, tremor, hypertension, hyperglycemia, gingival hyperplasia, hirsutism
Drug Interactions	Substrate of CYP3A4 and P-glycoprotein; inhibitor of CYP2C9, CYP3A4, and P-glycoprotein
Monitoring	Blood pressure, renal function, plasma concentrations, electrolytes, hepatic function, lipid profile
Case Notes	Cyclosporine is used as a part of the immunosuppression regimen in kidney, liver, and heart transplants. It is also used in rheumatoid arthritis, psoriasis, allogeneic stem cell transplant, focal segmental glomerulosclerosis, severe lupus, and ulcerative colitis. Compared to tacrolimus, cyclosporine causes more hypertension and hyperlipidemia and less diabetes mellitus. Cyclosporine is dosed according to type of transplant, time since transplant, and local protocols. The different cyclosporine products are not bioequivalent, and patients should be maintained on the same product to prevent dramatic changes in serum concentrations. Serum levels should be monitored to help prevent toxicities including nephrotoxicity.

A 39-year-old African-American woman presents to the kidney transplant clinic for a routine follow-up visit. She has a past medical history of kidney transplantation three years ago secondary to glomerulonephritis. She has been feeling well and does not report any changes to her medication regimen since her previous visit.

Allergies: NKDA

Medications: Tacrolimus 1 mg capsule 3 po twice daily; mycophenolate mofetil 500 mg tablet 2 po twice daily; prednisone 5 mg tablet 1 po once daily; famotidine 20 mg tablet 1 po twice daily; calcium citrate 500 mg/vitamin D 200 IU tablet (OTC) 1 po twice daily

Physical Exam/Other Studies:

Wt 160 lb Ht 66 in T 98.1°F BP 131/78 HR 65 RR 18 O_2 sat 98%

Physical exam is unremarkable.

Na 143 K 4.4 Cl 101 CO_2 26 BUN 12 SCr 0.7 Glu 203 (fasting) WBC 7.8 Plt 283

Tacrolimus trough 15 ng/mL

Which of her medications is most likely contributing to her elevated blood glucose level?

Tacrolimus	Calcineurin inhibitor (cyclosporine, tacrolimus)
Mechanism of Action	Inhibits the production of IL-2 and other cytokines by T cells, leading to blocked T-cell proliferation through inhibition of calcineurin phosphatase activity
***Contraindications/* Precautions**	*Hypersensitivity to tacrolimus/*For use only by an experienced physician, infection, malignancy, anaphylaxis with the injection form, diabetes mellitus, hyperkalemia, nephrotoxicity, neurotoxicity, posterior reversible encephalopathy syndrome, myocardial hypertrophy, hematologic malignancies, hepatic impairment, hypertension, renal impairment
Adverse Effects	Diarrhea, nausea, hepatotoxicity, nephrotoxicity, tremor, headache, hypertension, hyperglycemia, hyperkalemia, hypomagnesemia
Drug Interactions	Substrate and inhibitor of CYP3A4 and P-glycoprotein
Monitoring	Renal function, hepatic function, electrolytes, glucose, blood pressure, tacrolimus levels
Case Notes	Tacrolimus can be used as a part of the immunosuppression regimen in kidney, liver, and heart transplants. New-onset diabetes after transplant is a common problem. While both tacrolimus and prednisone may lead to hyperglycemia, it is likely that this patient's higher tacrolimus level may be contributing the most to the hyperglycemia. It is possible that reducing the dose of tacrolimus while staying levels in the therapeutic range may reverse the hyperglycemia that this patient is experiencing. The therapeutic range of tacrolimus differs depending on time since transplant and is transplant center specific. There are many significant drug interactions with tacrolimus. Care should be taken whenever any medication is added or subtracted to consider the possible impact on tacrolimus serum concentrations. Calcineurin inhibitors are also associated with nephrotoxicity through vasoconstriction of the afferent arteriole, and close monitoring of renal function is important.

A 55-year-old African-American man with end-stage renal disease secondary to uncontrolled hypertension presents to the hospital after being notified that he will be the recipient of a deceased donor kidney transplant. He has been undergoing peritoneal dialysis for the past year without any complications.

Allergies: Sulfa (rash)

Medications: Amlodipine 10 mg tablet 1 po once daily; lisinopril 20 mg tablet 1 po once daily; aspirin 81 mg tablet (OTC) 1 po once daily; calcium carbonate 500 mg tablet (OTC) 2 po with each main meal

Physical Exam/Other Studies:

Wt 180 lb Ht 70 in T 97.1°F BP 132/88 HR 63 RR 18 O_2 sat 98%

Physical exam is unremarkable.

Na 141 K 4.8 Cl 101 CO_2 22 BUN 23 SCr 9.7 Ca 8.4 PO_4 6 WBC 8.8 Hg 11

Panel reactive antibodies 20% Cross-match negative HLA typing three-antigen match

The transplant surgeon has prepared the preoperative orders and asks for your help in designing an appropriate pre- and intraoperative regimen for this patient. She has indicated that the patient will receive mycophenolate mofetil 1,000 mg orally and cefazolin 1 g intravenously prior to surgery. During surgery, the patient will receive methylprednisolone 1,000 mg intravenously.

What other therapy could be given during surgery to help prevent acute rejection?

Antibody Therapy	Antithymocyte globulins (equine polyclonal antibody, rabbit polyclonal antibody), interlukin-2 receptor antagonists (monoclonal antibodies: basiliximab, daclizumab), CD3 receptor monoclonal antibody (muromonab-CD3), alemtuzumab (monoclonal antibody)
Mechanism of Action	Polyclonal antibodies bind to a wide array of lymphocyte receptors resulting in lymphocyte depletion and immune suppression. The monoclonal antibodies are more specific for targeting a single receptor on T cells. The particular receptor depends on the nature of the agent and the target of the antibody. Please refer to the specific agents for more detailed information.
***Contraindications/* Precautions**	Please refer to specific agents for more detailed information. *Hypersensitivity to the agent, severe reaction to previous use/*Hypersensitivity and anaphylactic reactions, hematologic toxicity, infections, lymphoproliferative disorders, should only be used by an experienced physician
Adverse Effects	Hypersensitivity, anaphylaxis, infusion-related reactions, myelosuppression
Drug Interactions	Antithymocyte globulins can interfere with the immune response to live vaccines; interlukin-2 receptor antagonists may increase cyclosporine and tacrolimus concentrations
Monitoring	Infusion reactions, CBC, renal function, signs/symptoms of infection
Case Notes	Antibody therapy may be used as part of an induction regimen in kidney transplant recipients, especially those at a higher risk of acute rejection (African-Americans, deceased donor recipients, patients with panel reactive antibodies greater than 20%). Induction therapy may also be useful in delaying the time to initiation of cyclosporine or tacrolimus until the renal function has improved. These agents may also be used in treating acute rejection. The doses and agents used vary depending on the transplant center. The monoclonal antibodies may be used more frequently due to a lower rate of adverse events.

A 62-year-old woman presents to the emergency room complaining of redness, swelling, and drainage from an abdominal incision. Two weeks ago, she had an open cholecystectomy. Her past medical history includes a living donor kidney transplant five years ago and hypertension.

Allergies: NKDA

Medications: Amlodipine 10 mg tablet 1 po once daily; lisinopril 20 mg tablet 1 po once daily; aspirin 81 mg tablet (OTC) 1 po once daily; sirolimus 2 mg tablet 2 po once daily; mycophenolate mofetil 500 mg tablet 2 po twice daily

Physical Exam/Other Studies:

Wt 145 lb Ht 62 in T 99.1°F BP 135/89 HR 65 RR 20 O_2 sat 98%

Physical exam reveals erythema and purulent drainage at the incision site.

Na 141 K 4.8 Cl 101 CO_2 22 BUN 23 SCr 1.2 WBC 10.1

She is diagnosed with a postoperative wound infection and started on appropriate antimicrobial therapy.

Which of her medications may be contributing to the development of a postoperative wound infection?

Sirolimus	Mammalian target of rapamycin inhibitor (everolimus, sirolimus)
Mechanism of Action	Inhibits the regulatory kinase, mammalian target of rapamycin, suppressing cytokine-mediated T-cell proliferation.
Contraindications/ **Precautions**	*Hypersensitivity to the agent or any component of the formulation/*Limit use to experienced physicians, infection, not recommended for liver or lung transplants, malignancy, anaphylactic or hypersensitivity reactions, angioedema, interstitial lung disease, hyperlipidemia, lymphocele/fluid accumulation, proteinuria, renal effects, wound dehiscence/healing, hepatic impairment
Adverse Effects	Myelosuppression, hyperlipidemia, hypertriglyceridemia, delayed wound healing, mouth ulcers, increased liver enzymes, hypertension, rash, diarrhea, arthralgias, edema
Drug Interactions	Substrate of CYP3A4, P-glycoprotein, inhibits CYP3A4
Monitoring	Liver function, CBC, sirolimus or everolimus levels, serum cholesterol, triglycerides, blood pressure, renal function, urinary protein
Case Notes	The mammalian target of rapamycin inhibitors are used most commonly in kidney transplant recipients either in combination with cyclosporine and corticosteroids or after withdrawal of cyclosporine in low-moderate immunologic risk patients. Combination therapy with mycophenolate can be used to avoid the nephrotoxicity associated with calcineurin inhibitors. There are many warnings and precautions associated with the use of these agents and the reader is encouraged to refer to package information for each individual agent. Both agents can be associated with delayed wound healing and dehiscence. Everolimus is also indicated for use in renal cancer. Dosing of the agents depends on time since transplant, concomitant medications, and serum drug levels.

A mother who is a regular cutsomer at your pharmacy calls you on the phone and is panicked. She tells you that her 13-year-old daughter was playing outside in the yard and stepped on a wasp. She started itching and developed hives, but then it turned into facial edema, difficulty breathing, and choking. She has a past medical history of asthma and seasonal allergies. The mother needs your advice on what can be done to help her daughter recover from this wasp sting.

Allergies: Sulfa (rash), bananas (hives), nuts (hives)

Medications: Fluticasone/salmeterol 250/50 mcg diskus 1 inhalation twice daily; albuterol HFA inhaler 1-2 puffs po every four to six hours PRN for wheezing and SOB; mometasone 50 mcg nasal spray, two sprays in each nostril daily; cetirizine 10 mg tablet (OTC) 1 po every night

Physical Exam/Other Studies:

Wt 98 lb Ht 62 in

You determine she is suffering from an anaphylactic reaction to the wasp sting and recommend that she immediately seek emergency care. What medication does this patient need to treat her anaphylaxis?

Epinephrine	Alpha and beta agonist
Mechanism of Action	Stimulates alpha-, $beta_1$-, and $beta_2$-adrenergic receptors resulting in relaxation of smooth muscle in the bronchial tree, cardiac stimulation, and dilation of skeletal muscle vasculature
***Contraindications/* Precautions**	There are no absolute contraindications when using injected epinephrine in a life-threatening situation. *Narrow-angle glaucoma, shock, during general anesthesia with halogenated hydrocarbons, individuals with organic brain damage, with local anesthesia of the digits, during labor, heart failure, or coronary insufficiency/*Cardiovascular disease, cerebrovascular disease, diabetes, Parkinson's disease, thyroid disease, use with caution patients taking MAOIs or TCAs
Adverse Effects	Angina, hypertension, flushing, tachycardia, vasoconstriction, anxiety, headache, dizziness, tremor, weakness, dyspnea, pulmonary edema, diaphoresis
Drug Interactions	Epinephrine may increase levels of bromocriptine, sympathomimetics; levels of epinephrine may be increased by beta-blockers, COMT inhibitors, MAO inhibitors, serotonin/norepinephrine reuptake inhibitors, TCAs; combination with ephedra and yohimbe may cause CNS stimulation
Monitoring	Pulmonary function, heart rate, blood pressure, resolution of symptoms
Case Notes	Epinephrine is the gold standard of treatment for anaphylaxis. Epinephrine used for anaphylaxis is dispensed in a pen and is used intramuscularly, typically in the anterolateral aspect of the thigh at a dose of 0.3 mg for adults and 0.15 mg for children weighing 15-29 kg. Intramuscular injection into the buttocks should be avoided. If symptoms persist, the dose may be repeated in 5-15 minutes. The World Health Organization recommends that a patient with a history of severe allergic reactions should have one epinephrine dose for every 10-20 minutes of travel time to a medical emergency facility. To further aid in the symptoms of anaphylaxis, diphenhydramine and acetaminophen can also be administered to the patient.

A 24-year-old woman presents to her primary care physician complaining of painful urination for the past two days. Upon further questioning, she reports increased urinary frequency and urgency for the past two days without fever, chills, vomiting, or back pain. This is the first time she has ever had this problem. She has been sexually active with one partner for the past three months and uses condoms for contraception. Her last menstrual period was three weeks ago.

Allergies: NKDA

Medications: No routine medications

Physical Exam/Other Studies:

Wt 125 lb Ht 70 in T 98.6°F BP 104/78 HR 63 RR 12 O_2 sat 98%

Physical exam reveals no costovertebral angle tenderness, no vaginal discharge or lesions, and mild suprapubic tenderness.

Urinalysis shows the following: color: yellow; appearance: cloudy; WBC: 10-25 cells; leukocyte esterase: positive; nitrite: positive; many bacteria present.

The patient is diagnosed with acute uncomplicated cystitis.

What medication would be appropriate for the treatment of this urinary tract infection?

Sulfamethoxazole-Trimethoprim	Sulfonamide derivative (sulfisoxazole and sulfadiazine)
Mechanism of Action	Sulfamethoxazole (SMZ) interferes with bacterial folic acid synthesis and growth via inhibition of dihydrofolic acid formation. Trimethoprim (TMP) inhibits dihydrofolic acid reduction to tetrahydrofolate resulting in sequential inhibition of enzymes of the folic acid pathway.
***Contraindications*/Precautions**	*Hypersensitivity to sulfa or trimethoprim, megaloblastic anemia due to folate deficiency, infants <2 months old, severe hepatic or renal disease in an unmonitored patient, pregnancy (at term), breastfeeding*/Patients with G6PD deficiency, the elderly, and those with folate deficiency
Adverse Effects	Nausea, vomiting, anorexia, rash, urticaria; rarely: severe dermatologic reactions, blood dyscrasias, hepatotoxicity
Drug Interactions	SMZ may enhance the effects of warfarin; TMP may decrease the excretion of dofetilide; sulfonamides may enhance the toxicities of methotrexate.
Monitoring	Follow culture and sensitivity information to direct therapy. Monitor CBC, potassium, creatinine, and BUN.
Case Notes	The most common cause of uncomplicated urinary tract infection is *Escherichia coli*. Three-day therapy with SMZ-TMP or a fluoroquinolone is superior to single-dose therapy and should be the treatment of choice. Alternatively, nitrofurantoin can also be used as a five-day treatment. In this patient, 1 double-strength po BID SMZ-TMP would be the better choice for a short-course regimen since the pregnancy status is not available (eliminating the use of fluoroquinolones). The patient should be advised to take the mediation with a full glass of water. Pyridium may be useful in treating her dysuria. SMZ-TMP is also used in other infections including (but not limited to) skin and soft tissue infections, otitis media, opportunistic infections in immunocompromised patients, and others.

An 8-year-old girl presents to her primary care physician complaining of sudden onset of a sore throat. She also complains of fever, headache, throat pain, and difficulty swallowing. Her 15-year-old sister was diagnosed with strep throat yesterday.

Allergies: Penicillin (hives)

Medications: None

Physical Exam/Other Studies:

Wt 60 lb Ht 48 in T 102.3°F

Physical exam reveals erythema and patchy exudates on the tonsils and enlarged tender anterior cervical lymph nodes.

Group A streptococcal rapid antigen detection test is positive.

What antibiotic should be prescribed for the treatment of this infection?

Macrolide	Azithromycin, erythromycin, clarithromycin
Mechanism of Action	Binds to the 50S ribosomal subunit blocking transpeptidation and inhibits RNA-dependent protein synthesis at the chain elongation step
***Contraindications*/ Precautions**	*Hypersensitivity to ketolides or macrolides*/Patients at risk for prolonged cardiac repolarization, hepatic impairment, myasthenia gravis, and severe renal impairment
Adverse Effects	Diarrhea, nausea, abdominal pain, cramping, rash, and rarely, QTc prolongation
Drug Interactions	Erythromycin: Substrate of CYP3A4 and P-glycoprotein; inhibitor of CYP3A4 and P-glycoprotein; Clarithromycin: Substrate of CYP3A4; inhibitor of CYP3A4 and P-glycoprotein; avoid use with other agents that may prolong the QTc interval
Monitoring	Signs and symptoms of infection, liver function tests, CBC
Case Notes	Patients with documented group A streptococcal pharyngitis should be treated with antimicrobial therapy to prevent rheumatic fever. Penicillin is the drug of choice for the treatment of this infection, but in patients with an allergy to penicillin, a macrolide may be used. The newer agents like azithromycin and clarithromycin are as effective as erythromycin and cause fewer adverse effects and have fewer drug interactions. For adults azithromycin is dosed 500 mg on day one and then 250 mg daily for days two through four while clarithromycin is dosed 250 mg twice daily for 10 days. Gastrointestinal complaints are common with erythromycin. Taking the medication with food can help alleviate some of these symptoms.

A 78-year-old has been complaining of abdominal pain, cramping, and frequent loose stools for the past three days. He was admitted to the skilled portion of a nursing home for rehabilitation following a stroke four months ago. He has a past medical history of chronic obstructive pulmonary disease and hypertension in addition to the stroke. His rehabilitation efforts have been complicated by multiple infections for the past three months, and he has received the following antibiotics during this time period: nitrofurantoin for a urinary tract infection, cephalexin followed by clindamycin for cellulitis, and azithromycin for acute exacerbation of chronic bronchitis. The nursing staff is concerned about his new symptoms.

Allergies: NKDA

Medications: Clopidogrel 75 mg tablet 1 po once daily; amlodipine 10 mg tablet 1 po once daily; lisinopril 20 mg tablet 1 po once daily; salmeterol/fluticasone 500/50 mcg diskus 1 inhalation twice daily; albuterol MDI 2 puffs every six hours prn shortness of breath; tiotropium 18 mcg capsules 1 inhalation once daily

Physical Exam/Other Studies:

Wt 182 lb Ht 70 in T 102.3°F BP 110/52 HR 112 RR 23 O_2 sat 88%

Physical exam reveals a soft, non distended abdomen with diffuse tenderness to palpation. There is slight rebound and guarding as well as hyperactive bowel sounds.

WBC 35.1

A stool sample is collected.

Based on recent antibiotic use, the patient is at high risk for *Clostridium difficile* infection (CDI).

Which of the antibiotics used in this patient has a high risk of causing *Clostridium difficile* infection?

A. azithromycin C. clindamycin

B. cephalexin D. nitrofurantoin

Clindamycin	Lincosamide (lincomycin)
Mechanism of Action	Inhibits bacterial protein synthesis through reversible binding to the 50S ribosomal subunit to prevent peptide bond formation
***Contraindications*/ Precautions**	*Hypersensitivity to clindamycin or lincomycin*/Patients with gastrointestinal disease, hepatic impairment, and atopic patients
Adverse Effects	Diarrhea, pseudomembranous colitis, rash, and rarely, elevations in liver function tests
Drug Interactions	Diminishes the effect of erythromycin (avoid combination), may enhance the effects of neuromuscular-blocking agents
Monitoring	Signs/symptoms of infection, diarrhea, and with prolonged therapy, CBC, liver, and renal function
Case Notes	Although most antibiotics have been implicated in CDI, clindamycin is the agent most commonly associated with CDI, and patients should be educated to watch for any changes in bowel habits. Clindamycin is used in the treatment of anaerobic infections, skin and skin-structure infections, and infections caused by streptococci, staphylococci, and pneumococci. It also may be used in the treatment of community-acquired MRSA infections. It is typically dosed orally 150-450 mg every six to eight hours or via the IV or IM route, 1.2-2.7 g/day every 6-12 hours for adults. The vaginal cream and suppository are used in the treatment of bacterial vaginosis, and the topical forms are used in the treatment of acne. Patients with previous pseudomembranous colitis, regional enteritis, or ulcerative colitis should not use the topical or vaginal products.

A 33-year-old man has been hospitalized and intubated for the past week in the surgical intensive care unit following a motor vehicle accident. He had massive intra-abdominal trauma requiring multiple trips to the operating room. Over the past 24 hours, he has had several episodes of decreased oxygen saturations, requiring increases in his ventilator settings, and he has had copious secretions from his endotracheal tube.

Allergies: Ciprofloxacin (rash)

Medications: Enoxaparin 40 mg injection subcutaneously daily; famotidine 20 mg injection twice daily; docusate 100 mg tablet 1 per tube twice daily; fentanyl intravenous drip titrated for pain; midazolam intravenous drip titrated for sedation

Physical Exam/Other Studies:

Wt 172 lb Ht 70 in T 102.3°F BP 138/80 HR 70 RR 18 O_2 sat 78%

Physical exam reveals decreased breath sounds on the right.

SCr 0.6 WBC 15.1

Portable chest x-ray demonstrates a new right lower lobe infiltrate.

Blood, urine, and sputum cultures are pending.

The team is worried that the patient is developing ventilator-associated pneumonia.

What antibiotic should he receive in addition to piperacillin/tazobactam and vancomycin for empiric therapy?

Aminoglycosides	Gentamicin, tobramycin, amikacin, streptomycin
Mechanism of Action	Interferes with protein synthesis by binding to the 30S and 50S ribosomal subunits
***Contraindications*/ Precautions**	*Hypersensitivity to aminoglycosides*/Patients with vertigo, tinnitus, hearing loss, renal insufficiency, or neuromuscular disorders
Adverse Effects	Ototoxicity, nephrotoxicity, neurotoxicity
Drug Interactions	Medications that may cause ototoxicity or nephrotoxicity; aminoglycosides may enhance the respiratory depressing effects of neuromuscular-blocking agents
Monitoring	Culture and sensitivity information, urine output, BUN, SCr, hearing test (for patients on therapy longer than two weeks), and serum drug levels
Case Notes	Empiric therapy for patients with ventilator-associated (or healthcare-associated) pneumonia typically includes a triple-drug regimen with two antipseudomonal agents and an agent directed at resistant Gram-positive organisms. In this case, the patient was already receiving the antipseudomonal agent, piperacillin/tazobactam, and the anti staphylococcal agent, vancomycin. Therefore, this patient needs another antipseudomonal antibiotic such as an aminoglycoside or a fluoroquinolone. This patient has a ciprofloxacin allergy, so an aminoglycoside was the best choice. Once culture and sensitivity results are available, the regimen can be adjusted to direct therapy at the microorganism isolated. Aminoglycoside dosing must be individualized according to the patient's ideal body weight (dosing weight for obesity) and renal function. Two dosing schemes are commonly used: traditional dosing (given every 8-12 hours) and extended interval dosing (given every 24 hours). Regardless of the regimen selected, serum drug levels (peak and trough with traditional dosing) must be monitored due to the narrow therapeutic range. The dosing of amikacin is higher than the dosing of gentamicin or tobramycin. Streptomycin is typically reserved for use in multidrug-resistant infections such as tuberculosis.

A 40-year-old man presents to his physician complaining of a round, expanding skin lesion, fever, body aches, and fatigue for the past two days. About one week ago, the patient was deer hunting in the woods of rural Connecticut. After he returned home, he removed several ticks from his leg and groin area.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 192 lb Ht 70 in T 103°F BP 113/73 HR 60 RR 18 O_2 sat 98%

Physical exam reveals a warm, tender bull's eye lesion on the right leg. It is approximately 7 cm in diameter.

The patient is diagnosed with early Lyme disease.

What would be the best treatment for his infection?

Doxycycline	Tetracycline (doxycycline, minocycline, tetracycline)
Mechanism of Action	Inhibition of protein synthesis through binding to the 30S and potentially 50S ribosomal subunit; potentially alters the cytoplasmic membrane
***Contraindications*/ Precautions**	*Hypersensitivity to doxycycline or other tetracyclines*/Avoid use in children ≤8 years old due to tissue hyperpigmentation, enamel hypoplasia, and permanent tooth discoloration; avoid use in pregnancy (category D) due to tooth development concerns as well as possible retardation of skeletal development and reduced bone growth
Adverse Effects	Gastrointestinal upset, photosensitivity, rash, skin hyperpigmentation, urticaria, increased BUN, hepatotoxicity, and rarely esophagitis
Drug Interactions	Antacids, bile acid sequestrants, calcium salts, bismuth, iron salts, magnesium salts, quinapril, and sucralfate may decrease the absorption of tetracycline agents. Barbiturates, carbamazepine, and phenytoin may decrease the serum concentration of tetracyclines. Tetracyclines may enhance the neuromuscular-blocking agents, retinoic acid derivatives, and vitamin K antagonists. Tetracyclines may diminish the effects of penicillins.
Monitoring	Signs and symptoms of infection, CBC, liver, and renal function
Case Notes	Doxycycline is the drug of choice for most tick-borne illnesses including Lyme disease. It is almost 100% bioavailable and can usually be given orally for most infections. The adult dose is typically 100 mg twice daily. Although food may decrease levels slightly, these agents can be given with food to decrease the GI upset. Patients should drink a full glass of water and remain upright for 30 minutes to reduce the risk of esophageal irritation and ulceration. The tetracyclines also have activity against a wide variety of organisms and are used in the treatment of community-acquired pneumonia, acne, skin and soft tissue infections, and many others.

A 58-year-old woman presents to her primary care physician complaining of shortness of breath for the past two days. She also reports fever, chills, and coughing up a lot of mucous during the same time period. Her past medical history is significant for diabetes mellitus Type 2 and systolic heart failure.

Allergies: NKDA

Medications: Carvedilol 12.5 mg tablet 1 po twice daily; lisinopril 20 mg tablet 1 po once daily; metformin 500 mg tablet 1 po twice daily; aspirin 81 mg tablet (OTC) 1 po once daily; furosemide 20 mg tablet 2 po twice daily

Physical Exam/Other Studies:

Wt 192 lb Ht 62 in T 100.3°F BP 135/77 HR 102 RR 32 O_2 sat 88%

Physical exam reveals: tachypnea, coarse rhonchi throughout the left lung field

SCr 0.7 WBC 10.1

Chest x-ray reveals left lower lobe infiltrate.

The physician diagnoses her with acute community-acquired pneumonia.

What would be the best single-antibiotic regimen to treat her infection?

Respiratory Fluoroquinolones (FQ)	Gemifloxacin, levofloxacin, moxifloxacin
Mechanism of Action	Inhibition of DNA-gyrase results in inhibition of the relaxation of supercoiled DNA and promotion of DNA strand breakage. Moxifloxacin and gemifloxacin also inhibit topoisomerase IV.
***Contraindications*/ Precautions**	*Hypersensitivity to fluoroquinolones or any component of the formulation*/Boxed warning for tendon rupture/inflammation; altered cardiac conduction, CNS stimulation, glucose regulation, hypersensitivity reactions, peripheral neuropathy, photosensitivity, superinfection, may exacerbate myasthenia gravis, renal impairment, rheumatoid arthritis, seizures, elderly, and G6PD deficiency. Pediatric safety and efficacy have not been established.
Adverse Effects	Headache, nausea, diarrhea, dizziness, rash; rarely: hepatotoxicity
Drug Interactions	Antacids, calcium salts, iron salts, magnesium salts, sevelamer, sucralfate, and zinc salts may decrease the absorption of FQ; didanosine and quinapril may decrease the concentration of FQ; FQ may enhance effects of corticosteroids, vitamin K antagonists, insulin, and sulfonylureas; FQ may decrease the serum concentration of mycophenolate; NSAIDs may enhance the neuroexcitatory and seizure potential of FQ and increase the serum concentration of FQ; avoid agents that may prolong the QTc interval.
Monitoring	Signs and symptoms of infection, hepatic and renal function
Case Notes	A respiratory FQ would be the best choice for this patient according to the 2007 IDSA Treatment Guidelines for community-acquired pneumonia due to her co morbid conditions. Alternatively, the combination of a beta-lactam and a macrolide may also be used. Patients should be educated about the risk of tendon inflammation or rupture with FQ. Those at highest risk are patients on corticosteroids, organ transplant recipients, and patients >60 years old. There are numerous precautions and drug interactions that should be screened for prior to starting therapy with FQ.

A 21-year-old woman presents for a routine physical examination prior to a medical mission trip to Central America. She has no significant past medical history but is concerned about developing traveler's diarrhea while on her trip.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 132 lb Ht 64 in T 97.8°F BP 116/77 HR 68 RR 16 O_2 sat 98%

Negative urine pregnancy test

In addition to educating the patient regarding prevention of traveler's diarrhea, what antibiotic could be prescribed for her to self-administer if she develops diarrhea while on her trip?

Ciprofloxacin	Fluoroquinolone (ciprofloxacin, levofloxacin, ofloxacin, moxifloxacin, gemifloxacin)
Mechanism of Action	Inhibition of DNA-gyrase results in inhibition of the relaxation of supercoiled DNA and promotion of DNA strand breakage. Moxifloxacin and gemifloxacin also inhibit topoisomerase IV.
***Contraindications*/ Precautions**	*Hypersensitivity to ciprofloxacin, fluoroquinolones, or any component of the formulation, and concurrent use of tizanidine*/Boxed warning for tendon rupture/inflammation; altered cardiac conduction, CNS stimulation, glucose regulation, hypersensitivity reactions, peripheral neuropathy, photosensitivity, superinfection, may exacerbate myasthenia gravis, renal impairment, rheumatoid arthritis, seizures, elderly, and G6PD deficiency
Adverse Effects	Headache, nausea, diarrhea, dizziness, and rash; rarely: hepatotoxicity
Drug Interactions	Antacids, calcium salts, iron salts, magnesium salts, sevelamer, sucralfate, and zinc salts may decrease the absorption of fluoroquinolones (FQ); didanosine and quinapril may decrease the concentration of FQ; FQ may enhance effects of corticosteroids, vitamin K antagonists, insulin, and sulfonylureas; FQ may decrease the serum concentration of mycophenolate; NSAIDs may enhance the neuroexcitatory and seizure potential of FQ and increase the serum concentration of FQ; avoid agents that may prolong the QTc interval; ciprofloxacin is an inhibitor of CYP1A2.
Monitoring	Signs and symptoms of infection, hepatic and renal function
Case Notes	Ciprofloxacin (500 mg po BID × 3 days) or levofloxacin (500 mg po × 1 dose) is the drug of choice for the treatment of traveler's diarrhea (often caused by *E coli*). Azithromycin may be an alternative depending on the country involved. Compared to the other FQ, ciprofloxacin has more Gram-negative activity (including *P aeruginosa*) and is used in urinary tract infections, intra-abdominal infections (with metronidazole), and nosocomial pneumonia, among others.

A 15-year-old girl presents to her primary care physician complaining of sudden onset of a sore throat. She also complains of fever and aches and difficulty swallowing.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 102 lb Ht 60 in T 102.3°F

Physical exam reveals erythema and patchy exudates on the tonsils with enlarged tender anterior cervical lymph nodes.

Group A streptococcal rapid antigen detection test is positive.

What antibiotic should be prescribed for the treatment of this infection?

Natural Penicillins	Oral: penicillin VK; IM: penicillin benzathine; IV: penicillin G
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins inhibiting the final step of peptidoglycan synthesis of the cell wall
***Contraindications*/ Precautions**	*Hypersensitivity to amoxicillin, penicillin, or other beta-lactams/*Asthmatics, patients with renal failure, and those with a history of seizures
Adverse Effects	Rash, nausea, vomiting, diarrhea
Drug Interactions	Tetracyclines may diminish the effect of penicillins; probenecid may increase the serum concentrations of penicillins; penicillins may decrease the excretion of methotrexate; penicillins may decrease the concentration of the active metabolite of mycophenolate
Monitoring	Signs and symptoms of infection, renal and hepatic function, signs of anaphylaxis
Case Notes	Patients with documented group A streptococcal pharyngitis should be treated with antimicrobial therapy to prevent rheumatic fever. Penicillin is the drug of choice for the treatment of this infection, although amoxicillin is often used in children due to its better taste and the possibility of once-daily dosing. Penicillin should be given orally 250 mg three times daily or 500 mg twice daily for 10 days for adults and 50 mg/kg/day divided in three doses for children. Patients should take the medication on an empty stomach for best absorption. Penicillin benzathine may also be given as a one-time IM dose of 1.2 million units for adults. Penicillin is also used in the treatment of skin and soft tissue infections caused by *Streptococcus pyogenes*, and it remains the drug of choice in the treatment of syphilis.

A mother brings her 6-month-old daughter to the pediatrician complaining that the child has been increasingly irritable the past two nights. In addition, she has not been taking her feedings as well as usual and has a runny nose and cough. This morning, the mother noted a temperature of 101.4°F. The baby has a normal birth history and has otherwise been healthy. She is formula fed and is not exposed to cigarette smoking. She does attend a day care center during the week.

Allergies: NKDA

Medications: No routine medications

Physical Exam/Other Studies:

Wt 17 lb Ht 25 in T 102.3°F BP 90/60 HR 100 RR 30

Physical exam reveals a thickened and bulging gray eardrum on the right.

The pediatrician diagnoses the baby with acute otitis media (AOM).

What antibiotic should be prescribed to treat this infection?

Aminopenicillin	PO: amoxicillin, amoxicillin/clavulanate; IV: ampicillin, ampicillin/sulbactam
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins, inhibiting the final step of peptidoglycan synthesis of the cell wall
***Contraindications*/ Precautions**	*Hypersensitivity to amoxicillin, penicillin, or other beta-lactams*/Asthma patients, mononucleosis patients, and those with renal impairment. Chewable tablets contain phenylalanine.
Adverse Effects	Rash, nausea, vomiting, diarrhea, and rarely anaphylaxis
Drug Interactions	Tetracyclines may diminish the effect of penicillins; probenecid may increase the serum concentrations of penicillins; penicillins may decrease the excretion of methotrexate; penicillins may decrease the concentration of the active metabolite of mycophenolate.
Monitoring	Signs and symptoms of infection, signs of anaphylaxis, renal, hepatic, and hematologic function
Case Notes	Viruses are the most common cause of AOM. Bacterial causes include: *Streptococcus pneumoniae, Haemophilus influenzae,* and *Moraxella catarrhalis*. The treatment of AOM has evolved over time, and for children >6 months, who are afebrile and have no ear pain, antibiotics may be withheld. For those <6 months, antibiotic treatment is indicated. If the patient has not been on antibiotics in the past month, high-dose (90 mg/kg/day) amoxicillin is the treatment of choice. If the patient has been on antibiotics in the past month, then extra-strength amoxicillin/clavulanate, cefdinir, cefpodoxime, cefprozil, or cefuroxime axetil would be recommended. Patients <2 years should be treated for 10 days, while those older than 2 years should receive five to seven days of therapy. If the patient has a beta-lactam allergy, then a macrolide or TMP-SMZ may be alternatives. Drug-resistant *S pneumoniae* (DRSP) is an increasing problem, especially in those who are <2 years, have been on antibiotics in the past three months, and/or attend daycare. In the case of DRSP, a third-generation cephalosporin or even a fluoroquinolone (not approved for use in children, but when no other option exists they are appropriate) may be used.

A 33-year-old man presents to the emergency department complaining of redness and swelling to his left lower extremity. This has been increasingly getting worse over the past 36 hours. He believes that he was bitten by a spider after working in his basement. The emergency room physician notices a small abscess that has formed and performs an incision and drainage with cultures. Due to the high rate of MRSA in this community, the physician empirically places the patient on vancomycin and admits the patient to the hospital. Forty-eight hours later, the patient continues to complain of pain and swelling that has not improved much during treatment.

Allergies: NKDA

Medications: Vancomycin injection 1,000 mg intravenously every 12 hours

Physical Exam/Other Studies:

Wt 160 lb Ht 67 in T 98.6°F BP 120/70 HR 80 RR 18 O_2 sat 98%

Physical exam reveals a warm, erythematous left lower extremity.

The abscess culture taken in the emergency department is positive for methicillin-susceptible *Staphylococcus aureus* (MSSA).

The physician wants to de-escalate antibiotic therapy. What would be the best option to treat this infection?

Penicillinase-Resistant Penicillin	IV: oxacillin, nafcillin; PO: dicloxacillin, cloxacillin
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins inhibiting the final step of peptidoglycan synthesis of the cell wall
***Contraindications*/ Precautions**	*Hypersensitivity to penicillins*/Use with caution in asthmatics, patients with hepatic or renal dysfunction, superinfection
Adverse Effects	Nausea, vomiting, diarrhea, rash; rarely: neutropenia, agranulocytosis, hepatotoxicity
Drug Interactions	Tetracyclines may diminish the effect of penicillins; probenecid may increase the serum concentrations of penicillins; penicillins may decrease the excretion of methotrexate; penicillins may decrease the concentration of the active metabolite of mycophenolate; nafcillin is a CYP3A4 inducer.
Monitoring	Signs and symptoms of infection, monitor PT if patient is on warfarin, hepatic and renal function, hematologic function
Case Notes	The penicillinase-resistant penicillins (also known as the antistaphylococcal penicillins) are the drugs of choice for MSSA skin and soft tissue infections and endocarditis caused by MSSA. Their spectrum of activity is narrow, and they do not provide coverage against Gram-negative organisms. These agents typically do not have to be dose adjusted in patients with renal impairment. A disadvantage is that the intravenous formulations require frequent dosing (every four or six hours) and may often be given by continuous infusion. The intravenous forms also contain sodium, so caution should be exercised in using these agents in patients with heart failure.

A 63-year-old woman presents to the emergency department complaining of severe abdominal pain for the past day. She also reports fevers, chills, and sweats. She has a history of a partial colon resection 10 days ago after a recent diagnosis of colon cancer. Her past medical history is otherwise unremarkable.

Allergies: Sulfa

Medications: Docusate 100 mg tablet (OTC) 1 po twice daily; hydrocodone/acetaminophen 5/325 tablet 1 po every four to six hours prn pain

Physical Exam/Other Studies:

Wt 162 lb Ht 66 in T 100.8°F BP 106/77 HR 88 RR 18 O_2 sat 98%

Na 133 K 3.4 BUN 18 SCr 1.1 WBC 12.3 Hgb 11.1

CT scan of the abdomen is pending.

While waiting for the CT scan results, the emergency room physician wishes to initiate empiric antibiotics for the treatment of a possible intra-abdominal infection.

Which of the following single agents would be an appropriate choice for the treatment of this patient's possible healthcare-associated complicated intra-abdominal infection?

A. ceftriaxone
B. metronidazole
C. piperacillin/tazobactam
D. vancomycin

Piperacillin/Tazobactam	Extended-spectrum penicillin (piperacillin, piperacillin/tazobactam, ticarcillin, ticarcillin/tazobactam)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins, inhibiting the final step of peptidoglycan synthesis of the cell wall. Tazobactam inhibits many beta-lactamases including those produced by staphylococci.
***Contraindications*/ Precautions**	*Hypersensitivity to penicillins, beta-lactamase inhibitors, or any component of the formulation/*Anaphylactoid/ hypersensitivity reactions, bleeding disorders have been observed especially in patients with renal impairment, superinfection may occur, use with caution in patients with seizures, and watch for increased fever and rash in cystic fibrosis patients
Adverse Effects	Diarrhea, headache, rash, and rarely, thrombocytopenia
Drug Interactions	Tetracyclines may diminish the effect of penicillins; probenecid may increase the serum concentrations of penicillins; penicillins may decrease the excretion of methotrexate; penicillins may decrease the concentration of the active metabolite of mycophenolate; the extended-spectrum penicillins may decrease the serum concentrations of aminoglycosides.
Monitoring	Signs of anaphylaxis during first dose, signs and symptoms of infection, CBC, renal function, PT, PTT, signs of bleeding
Case Notes	The extended-spectrum penicillins are used for the treatment of moderate to severe infections including intra-abdominal infections. Piperacillin/tazobactam possesses activity against many Gram-positive (not MRSA), Gram-negative (including *P aeruginosa*), and anaerobic organisms and is considered a broad-spectrum antimicrobial agent. Since this patient has a recent history of intra-abdominal surgery, her abdominal infection would be hospital-acquired. The dosing range for piperacillin/tazobactam is 2.25-4.5 g IV every six to eight hours depending on renal function and infection type. It is often given by extended (four-hour) infusion.

A 78-year-old woman presents to the emergency room complaining of increasing shortness of breath and confusion. Three days ago, she was given sulfamethoxazole/trimethoprim to treat a urinary tract infection at her nursing home. This morning when the staff went to check on her, they discovered that she was very short of breath and confused. Her temperature was 103.1°F, and her blood pressure was 80/60 mmHg. She was transported to the emergency department for further evaluation and treatment.

Allergies: NKDA

Medications: Lisinopril 20 mg tablet 1 po once daily; hydrochlorothiazide 25 mg tablet 1 po once daily; lansoprazole 30 mg capsule 1 po once daily; multi vitamin tablet 1 po once daily; aspirin 81 mg tablet (OTC) 1 po once daily; docusate 100 mg tablet (OTC) 1 po twice daily

Physical Exam/Other Studies:

Wt 105 lb Ht 64 in T 102.3°F BP 78/62 HR 129 RR 30 O_2 sat 78%

Physical exam reveals decreased breath sounds bilaterally.

SCr 0.6 WBC 25.1

Portable chest x-ray demonstrates bilateral infiltrates in the lower lobes.

Blood, urine, and sputum cultures are pending.

The emergency room physician would like to initiate antibiotics for sepsis including vancomycin, gentamicin, and one other agent.

Which agent would not provide adequate coverage for this patient?

A. doripenem
B. ertapenem
C. imipenem/cilastatin
D. meropenem

Ertapenem	Carbapenem (imipenem/cilastatin, meropenem, and doripenem)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins inhibiting the final step of peptidoglycan synthesis of the cell wall
***Contraindications*/ Precautions**	*Hypersensitivity to ertapenem or other carbapenems, anaphylaxis reaction to other beta-lactam antibiotics*/CNS disorders such as brain lesions or a history of seizure, and renal impairment
Adverse Effects	Rash, headache, diarrhea, nausea, vomiting, and rarely, seizure (more common with imipenem/cilastatin)
Drug Interactions	Carbapenems may decrease the serum concentration of valproic acid/divalproex; probenecid may increase serum concentrations of carbapenems.
Monitoring	Signs/symptoms of infection, during prolonged therapy: renal function, liver function, hematologic function
Case Notes	Ertapenem is indicated for the treatment of moderate-to-severe infections such as complicated intra-abdominal infections, complicated skin and skin structure infections, and complicated urinary tract infection, and for prophylaxis during colorectal surgery. It provides antimicrobial activity against aerobic Gram-positive, aerobic Gram-negative, and anaerobic organisms, but it does not cover MRSA, *Enterococcus* sp, *Pseudomonas* sp, or *Acinetobacter* sp. Since the patient, in this case, would be at risk for multi drug-resistant organisms like *Pseudomonas* sp, ertapenem would not be the best carbapenem to add to her regimen. The other agents in this class have an extended spectrum of activity compared to ertapenem (including coverage of *Pseudomonas* sp). Ertapenem has a longer serum half-life compared to the other agents, allowing for once-daily dosing of 1 g (500 mg for Clcr <30 mL/min).

A 61-year-old woman has been hospitalized for the past six weeks following an intracranial hemorrhage. She has spent the entire hospitalization in the intensive care unit on mechanical ventilation. Her hospital course has been complicated by sepsis (resolved) and an ileus (resolved). She has been stable until the past 24 hours when she has become hypotensive, tachycardic, and febrile.

Allergies: Sulfa (rash)

Medications: Acetaminophen 650 mg suppository 1 rectally every six hours prn; docusate 150 mg/15 mL solution 100 mg per tube twice daily; levetiracetam 100 mg/mL solution 500 mg per tube every eight hours; metoclopramide 5 mg/mL injection 10 mg intravenously every six hours; pantoprozole injection 40 mg intravenously once daily

Physical Exam/Other Studies:

Wt 192 lb Ht 64 in T 102.3°F BP 78/47 HR 128 RR 22 O_2 sat 98% on ventilator

Physical exam demonstrates decreased breath sounds bilaterally.

BUN 40 SCr 3.5 WBC 15.3

Blood and sputum cultures are positive for *Klebsiella pneumoniae* that has been confirmed as an extended-spectrum beta-lactamase (ESBL) producer resistant to ceftazidime, aztreonam, and other third-generation cephalosporins.

What would be the best type of antibiotic to treat her infection?

Carbapenem	Doripenem, ertapenem, imipenem/cilastatin, meropenem
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins inhibiting the final step of peptidoglycan synthesis of the cell wall
***Contraindications*/ Precautions**	*Hypersensitivity to carbapenems, anaphylaxis reaction to other beta-lactam antibiotics/*CNS disorders such as brain lesions or a history of seizure, renal impairment, risk of superinfection
Adverse Effects	Rash, headache, nausea, vomiting, diarrhea, seizure (more common with imipenem/cilastatin)
Drug Interactions	Carbapenems may decrease the serum concentrations of divalproex and valproic acid; probenecid may increase the serum concentration of carbapenems; cyclosporine, valganciclovir, and ganciclovir may enhance the toxicities of imipenem; imipenem may increase or decrease the serum concentrations of cyclosporine
Monitoring	Signs and symptoms of infection, watch for anaphylaxis with first dose, renal, hepatic, and hematologic function tests
Case Notes	The carbapenems (particularly doripenem, imipenem/cilastatin, and meropenem) are the preferred agents to treat infections caused by ESBL-producing organisms that are resistant to ceftazidime and other third-generation cephalosporins. In this patient, meropenem or doripenem might be preferred due to her poor renal function and lowered seizure threshold from the intracranial hemorrhage. All of the carbapenems must be dose adjusted for renal dysfunction. Of increasing concern are *Klebsiella pneumoniae,* which produce carbapenemases (eliminating the use of carbapenems). Due to these multi drug-resistant strains, the use of carbapenems should be reserved for serious infections caused by Gram-positive (not MRSA), Gram-negative, or anaerobic organisms.

A 43-year-old woman presents to the emergency department complaining of abdominal pain. She was recently hospitalized for three days following a laparoscopic cholecystectomy. In the emergency department, she is noted to be hypotensive and tachycardic. She is given fluids and placed on a norepinephrine drip to maintain her blood pressure. She is sent to the intensive care unit with a diagnosis of sepsis.

Allergies: Amoxicillin (anaphylaxis)

Medications: No home medications

Physical Exam/Other Studies:

Wt 272 lb Ht 64 in T 97.5°F BP 85/55 HR 112 RR 24 O_2 sat 78%

Physical exam reveals no significant findings.

SCr 1.48 WBC 14.1 Lactic acid 5.1 INR 1.45

CT of the abdomen demonstrates a large pelvic abscess.

Blood culture: Gram stain is positive for non-lactose fermenting Gram-negative rods.

The physician initiates therapy with metronidazole and ciprofloxacin but wishes to provide the patient with double coverage for this Gram-negative bacteremia and pelvic abscess with an agent that interferes with the bacterial cell wall.

In addition to ciprofloxacin 400 mg IV and metronidzazole 500 mg IV every eight hours, what agent should be given?

Aztreonam	Monobactam (no other agents)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins, thus inhibiting the final step of peptidoglycan synthesis. This causes bacteria to lyse and cell-wall assembly to stop.
***Contraindications*/ Precautions**	*Hypersensitivity to aztreonam*/Use with caution in patients with penicillin or cephalosporin allergy as rare cross-allergy has been reported; use with caution in patients with renal insufficiency
Adverse Effects	Rash, diarrhea, nausea, vomiting, injection site reactions
Drug Interactions	No relevant interactions
Monitoring	Signs/symptoms of infection, signs of anaphylaxis during first dose
Case Notes	This patient has a history of anaphylaxis with amoxicillin, so penicillins and cephalosporins should be avoided. Aztreonam is an agent that may be used in patients with a history of anaphylaxis to penicillins or cephalosporins (except ceftazidime). Its spectrum of activity is narrow, covering Gram-negative organisms only. It is effective against *Pseudomonas aeruginosa*, and it can be used for urinary tract infections, respiratory tract infections, septicemia, and other Gram-negative infections. The typical dose is 500 mg, 2 g intravenously every 8-12 hours. It may also be given via the inhalational route in cystic fibrosis patients with *P aeruginosa.*

A 41-year-old woman presents to her primary care physician complaining of a swollen right forearm. She believes that she was bitten by a spider while cleaning out her basement two days ago. The area began to swell and has spread significantly in the past 24 hours. She is otherwise healthy.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 182 lb Ht 66 in T 98.3°F BP 135/86 HR 70 RR 16 O_2 sat 98%

The patient is diagnosed with right arm cellulitis.

Which of the following agents would be the best choice for initiating therapy for this patient?

A. cefdinir
B. cefixime
C. cefuroxime
D. cephalexin

Cephalexin	First-generation cephalosporin (IV: cefazolin, PO: cefadroxil, cephalexin)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins and inhibiting the final step of peptidoglycan synthesis
***Contraindications*/ Precautions**	*Hypersensitivity to cephalosporins, or any component of the formulation*/Use with caution in patients with IgE-mediated penicillin allergy; prolonged use may result in superinfection; use with caution in patients with renal impairment; may be associated with elevations in INR; use with caution in patients with seizure disorder (cefazolin)
Adverse Effects	Diarrhea, and rarely anaphylaxis and bone marrow suppression
Drug Interactions	Probenecid may increase the concentrations of cephalosporins; cephalosporins may enhance the anticoagulant effect of vitamin K antagonists; cephalexin may increase the serum concentration of metformin
Monitoring	Signs of anaphylaxis during first dose, signs and symptoms of infection, renal, hepatic, and hematologic function
Case Notes	The first-generation cephalosporins have a relatively narrow spectrum of activity. Of the cephalosporins, they have the best Gram-positive activity, but their Gram-negative activity is limited (sensitive strains of *E coli, Klebsiella* sp, *and Proteus* sp). Most cellulitis infections are caused by staphylococci or streptococci. As long as MRSA is not suspected, the first-generation agents are an appropriate choice for treating this type of infection. Other uses for the first-generation cephalosporins are in surgical infection prophylaxis, as an alternative in staphylococcal endocarditis, and for prophylaxis during dental procedures in patients at risk for endocarditis.

A 51-year-old man presents to the pre-op clinic one week before he is planning to undergo a revision of his colostomy. His past medical history is significant for Crohn disease, which has been well-controlled since his previous partial colectomy and hypertension.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 172 lb Ht 69 in T 97.3°F BP 129/87 HR 68 RR 14 O_2 sat 98%
SCr 0.89 Hgb 12.3

The nurse taking care of the patient realizes that the surgeon has forgotten to indicate the antibiotic for surgical infection prophylaxis for this patient. After placing a call to the surgeon, the nurse is asked to call the hospital pharmacy for a recommendation for this patient's surgical procedure.

Which of the following agents would provide appropriate coverage for surgical infection prophylaxis in a patient undergoing colon surgery?

A. cefazolin
B. cefoxitin
C. clindamycin
D. vancomycin

Cefoxitin	Cephamycin (cefotetan, cefoxitin)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins and inhibiting the final step of peptidoglycan synthesis
***Contraindications*/ Precautions**	*Hypersensitivity to cephamycins, other cephalosporins, or any component of the formulation*/Use with caution in patients with IgE-mediated penicillin allergy, prolonged use may result in superinfection, and use with caution in patients with renal impairment
Adverse Effects	Diarrhea and rarely: anaphylaxis and bone marrow suppression
Drug Interactions	Probenecid may increase the concentrations of cephalosporins; cephalosporins may enhance the anticoagulant effect of warfarin
Monitoring	Signs of anaphylaxis during first dose, signs and symptoms of infection, and renal function
Case Notes	Of the choices listed in the case, cefoxitin would be the agent that provides the best coverage for an intra-abdominal surgery. The cephamycins are a subclass of the second-generation cephalosporins. They have more Gram-negative activity compared to first-generation cephalosporins and also are active against anaerobes like *Bacteroides fragilis* so are often used for surgical infection prophylaxis. Due to concerns with increasing resistance to anaerobic organisms, their use is limited to surgical infection prophylaxis, and they are rarely used to treat an infection. Cefotetan contains the methyltetrazolethiol side chain, which may be associated with elevated INR and, when combined with alcohol, a disulfiram reaction. Both cephamycins may be used for prophylaxis during colon surgical procedures. Other appropriate options include: ampicillin/sulbactam, ertapenem, cefazolin plus metronidazole, cefuroxime plus metronidazole, clindamycin plus an aminoglycoside, clindamycin plus a quinolone, clindamycin plus aztreonam, metronidazole plus an aminoglycoside, or metronidazole plus a quinolone. All of these regimens provide activity against the enteric Gram-negatives and anaerobic organisms.

A 6-year-old girl is brought to the emergency department by her family. The mother states that the patient was in her usual state of health until she awoke this morning crying and complaining of a headache. The mother also states that the child was initially irritable but quickly became lethargic and has a new purple spot on her face and a rash on her arms and legs.

Allergies: NKDA

Medications: No routine medications

Physical Exam/Other Studies:

Wt 42 lb Ht 48 in T 104.3°F BP 90/60 HR 70 RR 32 O_2 sat 98%

Physical exam reveals: nuchal rigidity, lethargy, difficult to arouse, positive Brudzinski's and Kernig's signs, and a petechial rash on the extremities

WBC 18

Lumbar puncture: CSF glucose 20 CSF protein 250 CSF WBC 1,200 with 90% PMNs and 6% lymphocytes

Initial Gram stain of the CSF is positive for Gram-negative diplococci.

Based on the patient's presentation and laboratory findings, an initial diagnosis of meningitis is determined.

In addition to vancomycin, what empiric antimicrobial therapy should she receive?

Ceftriaxone or Cefotaxime	Third-generation cephalosporin (IV: ceftriaxone, cefotaxime, ceftizoxime, ceftazidime; PO: cefdinir, cefixime, cefpodoxime proxetil, ceftibuten, cefditoren pivoxil)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins and inhibiting the final step of peptidoglycan synthesis
***Contraindications*/ Precautions**	*Hypersensitivity to other cephalosporins; do not use ceftriaxone in hyperbilirubinemic neonates*/ Patients with PCN allergy (especially IgE-mediated reactions like anaphylaxis, angioedema, urticaria), concomitant hepatic and renal disease, and patients with a history of gastrointestinal disease
Adverse Effects	Rash, nausea, vomiting, diarrhea, and rarely: blood dyscrasias, *Clostridium difficile* colitis, red stools (cefdinir)
Drug Interactions	Ceftriaxone may complex with calcium, leading to precipitates—use with caution in neonates on calcium-containing solutions and do not administer to any patient at the same time as a calcium infusion; probenecid may increase the concentrations of cephalosporins; cephalosporins may enhance the anticoagulant effect of warfarin
Monitoring	Signs/symptoms of infection, anaphylaxis
Case Notes	In general, third-generation cephalosporins have improved Gram-negative activity compared to first- and second-generation agents. Like all cephalosporins, the third-generation agents do not have activity against enterococci, and only ceftazidime has reliable activity against *Pseudomonas* sp. Ceftriaxone and cefotaxime penetrate well into the CNS, so they are both choices for the empiric treatment of meningitis in this patient (in addition to vancomycin). Ceftriaxone has a long half-life and does not require renal dosing adjustments. The oral agents in this class are used for upper respiratory tract infections and uncomplicated skin and skin structure infections.

A 73-year-old man has been hospitalized for the past five days for an exacerbation of his chronic obstructive pulmonary disease (COPD). The exacerbation was severe enough that mechanical ventilation was initiated, and the patient has now been in the intensive care unit on the ventilator for the past five days. He was initially placed on antibiotics for the empiric treatment of a COPD exacerbation, but his condition worsened and the antibiotics were expanded to include coverage of nosocomial organisms. He has improved with this regimen.

Allergies: NKDA

Medications: Docusate 100 mg tablet 1 po bid; ciprofloxacin injection 400 mg intravenously every eight hours; meropenem injection 1 g intravenously every eight hours; vancomycin injection 1,250 mg intravenously every 18 hours; fentanyl intravenous drip titrated for pain and sedation; midazolam intravenous drip titrated for sedation; methylprednisolone injection 60 mg intravenously every 12 hours; famotidine injection 20 mg intravenously every 12 hours

Physical Exam/Other Studies:

Wt 182 lb Ht 70 in T 98.4°F BP 129/77 HR 78 RR 14 O_2 sat 98% (on ventilator)
BUN 22 SCr 1.25 WBC 11.2

A bronchoscopy was performed, and cultures were sent to the lab. The culture grew *Pseudomonas aeruginosa* that was sensitive to all agents tested. The pulmonologist wishes to de-escalate the antibiotic therapy.

Which of the following agents has coverage against *Pseudomonas aeruginosa* and could be used in treating this patient?

A. cefepime
B. ertapenem
C. moxifloxacin
D. tigecycline

Cefepime	Fourth-generation cephalosporin (no other agents)
Mechanism of Action	Inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins and inhibiting the final step of peptidoglycan synthesis
***Contraindications*/ Precautions**	*Hypersensitivity to cefepime, other cephalosporins, penicillins, other beta-lactam antibiotics, or any component of the formulation*/May be associated with increased INR, use with caution in patients with penicillin allergy, prolonged use may result in superinfection, use with caution in patients with a history of colitis, seizures, or renal insufficiency
Adverse Effects	Positive Coombs test, rash, and rarely: seizures, agranulocytosis
Drug Interactions	Probenecid may increase the concentrations of cephalosporins
Monitoring	Signs of anaphylaxis during first dose, signs and symptoms of infection, renal and hepatic function
Case Notes	Cefepime is one of only two currently available anti pseudomonal cephalosporins. The other is a third-generation agent, ceftazidime. Cefepime has a broad Gram-negative and Gram-positive spectrum of activity, but does not cover anaerobic organisms or MRSA, so is considered a narrower spectrum agent than carbapenems or extended-spectrum penicillins. It is often used in the treatment of febrile neutropenia and can also be used to treat brain abscesses. For the treatment of nosocomial pneumonia, it is dosed 500-2000 mg every 8-12 hours depending on renal function. An initial concern for increased mortality in cefepime-treated patients has been resolved by the FDA. The other agents listed as choices in the case do not have pseudomonal activity and would not be appropriate choices for treating this patient's infection.

A 56-year-old man calls your pharmacy concerned that the antibiotic that you dispensed three days ago is not working for him. The patient initially presented to his physician complaining of pain and swelling on his left calf from a spider bite. His past medical history is significant for Type 2 diabetes mellitus and hypertension. The physician diagnosed the patient with cellulitis and wrote a prescription for cephalexin 500 mg capsules 1 po four times daily. The patient has been adherent to this regimen for the past three days but feels that the wound on his leg is not improving. After consultation with you, he returns to his physician for re-evaluation. The physician determines that the cellulitis has worsened with the development of an abscess and admits the patient to the hospital for intravenous antibiotics.

Allergies: Sulfa (rash), erythromycin (rash), codeine (rash)

Medications: Metformin 1,000 mg tablet 1 po twice daily; aspirin 81 mg tablet (OTC) 1 po daily; lisinopril 20 mg tablet 1 po daily; hydrochlorothiazide 25 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 202 lb Ht 70 in T 98.6°F BP 142/83 HR 63 RR 16 O_2 sat 98%

Physical exam reveals left lower extremity redness, warmth, and tenderness.

BUN 23 SCr 0.9 WBC 26.3

Initial wound culture: *Staphylococcus aureus* (susceptibilities pending)

A surgical consult is ordered for incision and drainage of the abscess.

What empiric antimicrobial therapy should be ordered for this patient?

Glycopeptide	Vancomycin, telavancin
Mechanism of Action	Inhibits bacterial cell-wall synthesis by blocking polymerization and cross-linking of peptidoglycan
***Contraindications*/ Precautions**	*Hypersensitivity to vancomycin or patients with hearing loss (vancomycin only)*/Use telavancin cautiously with history of prolonged QTc interval. Caution with pre-existing renal impairment.
Adverse Effects	Vancomycin: hypotension, red man syndrome, Rarely: neutropenia, thrombocytopenia, renal failure, ototoxicity; Telavancin: insomnia, HA, psychiatric disorders, metallic/soapy taste, nausea and vomiting, foamy urine, thrombocytopenia, Rarely: hearing loss, QTc prolongation
Drug Interactions	Vancomycin may enhance the nephrotoxicity of other nephrotoxic agents. Telavancin should not be given with other agents that prolong the QTc interval.
Monitoring	Follow culture and sensitivity information to direct therapy. Monitor urine output, BUN, SCr, and serum vancomycin trough levels.
Case Notes	Since this patient has failed outpatient treatment with cephalexin and is growing *Staphylococcus aureus* from the wound culture, empiric therapy with vancomycin (or telavancin) would be appropriate to cover for potential MRSA. One of the most common adverse reactions experienced with vancomycin is red man syndrome, which is caused by histamine release. This can be alleviated and/or avoided by slowing down the rate of infusion. Current recommendations for vancomycin serum monitoring are to check vancomycin trough levels in patients on aggressive dosing, with unstable renal function, with concurrent nephrotoxins, or with a prolonged course of therapy. Target trough levels vary depending on indication. For most general infections, target trough levels of 10 mcg/mL or greater are appropriate. For more serious infections such as bacteremia, endocarditis, osteomyelitis, meningitis, and hospital-acquired pneumonia, levels of 15-20 mcg/mL are suggested.

A 33-year-old man has been hospitalized and intubated for the past week in the surgical intensive care unit following a motor vehicle accident. He had massive intra-abdominal trauma requiring multiple trips to the operating room. Over the past 24 hours, he has had several episodes of reductions in oxygen saturation and copious secretions from his endotracheal tube. The team started him on therapy with piperacillin/tazobactam, vancomycin, and gentamicin due to concerns for ventilator-associated pneumonia. Blood, urine, and sputum cultures were also collected. He has continued to have an elevated WBC and secretions from his endotracheal tube.

Allergies: Ciprofloxacin (rash)

Medications: Enoxaparin subcutaneous injection 40 mg daily; famotidine intravenous injection 20 mg twice daily; docusate 100 mg tablet 1 per tube twice daily

Physical Exam/Other Studies:

Wt 172 lb Ht 70 in T 102.3°F BP 138/80 HR 70 RR 18 O_2 sat 78%

Physical exam reveals decreased breath sounds on the right.

SCr 0.6 WBC 18.1 vancomycin trough level 5.2

Portable chest x-ray demonstrates a right lower lobe infiltrate.

Sputum culture is positive for methicillin-resistant *Staphylococcus aureus* (MRSA).

The team is worried that the low vancomycin level (<10) is leading to inadequate treatment for this patient.

What alternative antibiotic could you recommend for the treatment of this MRSA ventilator-associated pneumonia?

Oxazolidinone	Linezolid
Mechanism of Action	Inhibits bacterial protein synthesis through binding to the bacterial 23S ribosomal subunit of the 50S subunit and preventing formation of a functional 70S initiation complex
***Contraindications*/ Precautions**	*Hypersensitivity to linezolid, concurrent use or use within two weeks of using MAO inhibitors, uncontrolled hypertension, pheochromocytoma, thyrotoxicosis, carcinoid syndrome, sympathomimetics, vasopressors, dopaminergic agents, SSRIs, TCAs, 5-HT$_{1D}$ receptor agonists, meperidine, buspirone/*Patients with pre-existing myelosuppression or seizure disorder; oral suspension contains phenylalanine
Adverse Effects	Headache, diarrhea, thrombocytopenia (especially with treatment beyond 14 days); rarely: lactic acidosis, optic neuropathy, seizures, serotonin syndrome
Drug Interactions	Linezolid is a weak MAO inhibitor and should be used with caution with agents that have serotonergic, dopaminergic, and vasopressor activities due to the risk for serotonin syndrome. Avoid tyramine-rich foods and supplements containing caffeine, tyrosine, or tryptophan.
Monitoring	Signs and symptoms of infection, CBC, visual function (with treatment greater than three months)
Case Notes	Linezolid is an alternative for the treatment of MRSA pneumonia. It is typically given intravenously at a dose of 600 mg every 12 hours for seven days. Due to its lack of therapeutic drug monitoring, it is an attractive alternative to vancomycin. Due to its potential to cause serotonin syndrome when given with interacting agents, its use may be limited in certain patients on interacting medications. Linezolid may also be used for VRE infections and complicated skin/skin structure infections. With nearly 100% bioavailability, patients may be transitioned to an oral regimen with a dose of 600 mg po every 12 hours to continue therapy as out-patients if needed.

A 22-year-old pregnant woman presents to the emergency department complaining of increasing abdominal pain in her right upper quadrant. She describes moderate-to-severe pain that radiates to her right shoulder and is associated with nausea and vomiting. She is currently 28 weeks pregnant with her fourth child, and she has never experienced this type of pain in any previous pregnancy. Her medical history is significant for asthma.

Allergies: NKDA

Medications: Prenatal vitamin tablet (OTC) 1 po once daily; albuterol MDI 1 puff every four to six hours as needed

Physical Exam/Other Studies:

Wt 170 lb Ht 65 in T 99.3°F BP 125/76 HR 70 RR 16 O_2 sat 98%

Her physical exam is positive for right upper quadrant tenderness and a positive Murphy sign.

A gallbladder ultrasound is positive for a 10-11 mm stone that is dilating the common bile duct.

The patient is diagnosed with cholecystitis secondary to gallstone formation. Since she is pregnant, she will undergo an endoscopic retrograde cholangiopancreatography (ERCP) in the morning with the possibility of surgery if the ERCP is unsuccessful. Until then, the physician would like to start empiric antibiotics to cover her until the procedure.

Which of the following antibiotic regimens should not be used as empiric therapy for this patient?

A. piperacillin/tazobactam
B. cefotaxime and metronidazole
C. tigecycline
D. ticarcillin/clavulanate

Tigecycline	Glycylcycline (no other agents)
Mechanism of Action	Inhibits protein synthesis by binding to the 30S ribosomal subunit of bacteria
***Contraindications*/ Precautions**	*Hypersensitivity to tigecycline*/Antianabolic effects; hepatotoxicity; pancreatitis; photosensitivity; pseudotumor cerebri; prolonged use may result in superinfection; use with caution as monotherapy for intestinal perforation; do not use for nosocomial pneumonia; pregnancy category D; safety/efficacy for children <18 has not been established
Adverse Effects	Nausea, vomiting, diarrhea, increased LFTs, increased BUN
Drug Interactions	Tigecycline may increase the serum concentrations of warfarin.
Monitoring	Monitor for signs/symptoms of anaphylaxis with the first dose, monitor culture and sensitivity data to direct therapy, and liver function tests
Case Notes	Since this patient is pregnant and tigecycline is pregnancy category D, this would not be the best choice for the treatment of this patient's possible infection. Tigecycline is a minocycline derivative with an expanded spectrum of activity. It covers Gram-positive (including MRSA), Gram-negative (excluding *Pseudomonas*), and anaerobic organisms. However, there are some concerns with this agent. In phase 3 and 4 clinical trials, there was an increase in all-cause mortality. Also in patients with ventilator-associated pneumonia, there was a decrease in cure and increase in mortality. In patients with intestinal perforation, there was an increase in sepsis/septic shock. There have also been reports of development of bacteremias and resistance during treatment with tigecycline. Finally, tigecycline achieves very high concentrations in the tissues compared to plasma, creating a concern in using this agent to treat bacteremias. This agent should be reserved for use in patients with multi drug-resistant organisms who are intolerant to other available agents. In addition to adverse effects seen in pregnant animals, tigecycline has the potential to cause permanent tooth discoloration.

A 27-year-old man presents to the emergency department complaining of a sudden onset of shortness of breath and fever. He also complains of cough, chest pain, and fatigue. His past medical history is significant for frequent hospitalizations for MRSA abscesses. Upon further questioning, he admits to intravenous drug abuse and drinking binges on the weekends.

Allergies: Vancomycin (anaphylaxis)

Medications: No routine medications

Physical Exam/Other Studies:

Wt 162 lb Ht 68 in T 101.3°F BP 80/57 HR 116 RR 22 O_2 sat 88%

Physical exam is normal except for an ejection murmur that is best heard at the left sternal border.

SCr 0.5 WBC 17.1

Chest x-ray reveals nodular infiltrates diffusely.

Transthoracic echocardiogram shows a large vegetation on the tricuspid valve leaflet.

Four sets of blood cultures are positive for Gram-positive cocci in clusters at 12 hours.

He is given a diagnosis of right-sided infective endocarditis.

What would be the best antibiotic to treat his infection?

Daptomycin	Cyclic lipopeptide
Mechanism of Action	Daptomycin binds to the cell membrane and causes rapid depolarization, leading to inhibition of intracellular DNA, RNA, and protein synthesis.
***Contraindications*/ Precautions**	*Hypersensitivity to daptomycin*/Patients on medications associated with myopathy or in patients with neuropathy. Do not use in pneumonia since the drug is inactivated by pulmonary surfactant.
Adverse Effects	Nausea, vomiting, diarrhea, myopathy
Drug Interactions	HMG-CoA reductase inhibitors may increase the risk of myopathy.
Monitoring	Signs and symptoms of infection, CPK at weekly intervals, and monitoring for muscle pain or weakness
Case Notes	Daptomycin is bactericidal in a concentration-dependent manner. It is indicated for the treatment of complicated skin and skin structure infections and *Staphylococcus aureus* bacteremia including right-sided endocarditis caused by methicillin-susceptible or resistant *Staphylococcus aureus*. It may also be used in infections caused by vancomycin-resistant enterococci. The normal dose is 4 mg/kg once daily for patients with skin and skin structure infections and 6 mg/kg/day in patients with bacteremia or endocarditis. For patients with Clcr <30 mL/min or on dialysis, the dosing interval should be extended to every 48 hours. Daptomycin would be the best choice for this patient due to his vancomycin allergy and his history of MRSA infections.

A 22-year-old man has been hospitalized for the past six weeks following a motor vehicle accident. His injuries were vast including both head and abdominal injuries. He has been in and out of the operating room for repair of these injuries. Since admission, he has required mechanical ventilation and vasopressor support. He has recently completed a seven-day course of vancomycin for a MRSA ventilator-associated pneumonia. His chest x-ray has shown improvement, and his WBC has been decreasing. Today, he spiked a fever of 103°F and became more hypotensive, requiring increasing amounts of vasopressors.

Allergies: NKDA

Medications: Enoxaparin subcutaneous injection 40 mg daily; famotidine intravenous injection 20 mg twice daily; docusate 100 mg tablet 1 per tube twice daily; fentanyl intravenous drip titrated for pain; midazolam intravenous drip titrated for sedation; norepinephrine intravenous drip titrated for BP

Physical Exam/Other Studies:

Wt 152 lb Ht 70 in T 103.3°F BP 75/50 HR 110 RR 18 O_2 sat 78%

Physical exam is unremarkable except for the incisions on his abdomen.

Na 127 K 4.5 Cl 109 CO_2 23 BUN 11 SCr 0.6 WBC 19.1

Portable chest x-ray demonstrates improvement in the infiltrate compared to the previous day.

Blood, urine, and sputum cultures are ordered, and the initial blood cultures are positive for Gram-positive cocci in pairs and chains.

The patient is initiated on therapy with broad-spectrum antimicrobial agents including vancomycin, piperacillin/tazobactam, and gentamicin, but his status continues to deteriorate. Forty-eight hours later, the final blood culture results show that he is growing vancomycin-resistant *Enterococcus faecalis.*

Which antibiotic should not be recommended for treatment of vancomycin-resistant *Enterococcus faecalis*?

A. daptomycin
B. linezolid
C. quinupristin/dalfopristin
D. tigecycline

Quinupristin/ Dalfopristin	Streptogramin (no other agents in this class)
Mechanism of Action	Inhibits bacterial protein synthesis by binding to two sites on the 50S ribosomal subunit ultimately inhibiting protein synthesis
***Contraindications*/ Precautions**	*Hypersensitivity to quinupristin, dalfopristin, pristinamycin, or virginiamycin, or any component of the formulation*/Use only for vancomycin-resistant *Enterococcus faecium* infections; safety and efficacy have not been established in children younger than 16; use with caution in patients with hepatic dysfunction
Adverse Effects	Arthralgias, myalgias, hyperbilirubinemia, pain/phlebitis when infused through peripheral line
Drug Interactions	Use with cisapride may cause prolongation of the QT interval; quinupristin is a weak inhibitor of CYP3A4
Monitoring	Signs and symptoms of infection, bilirubin, liver function tests, symptoms of arthralgias/myalgias
Case Notes	Quinupristin/dalfopristin is typically reserved for use in serious or life-threatening infections caused by vancomycin-resistant *E faecium*. It may also have a place in the treatment of other infections such as complicated skin and soft tissue infections including those caused by methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* and *Streptococcus pyogenes.* For adults, the typical dose for serious infections is 7.5 mg/kg every eight hours and for skin infections 7.5 mg/kg every 12 hours. There are no dosing adjustments for renal or hepatic impairment, although use in patients with hepatic dysfunction is cautioned. Due to its potential for drug interactions and the side effects of arthralgias/myalgias, it is not a first-line agent. Tigecycline would cover the organism this patient is growing, but it is typically not used in bacteremias unless no other options are available.

A 73-year-old man presents to the clinic complaining of several days of frequent foul-smelling stools. He also complains of cramping and abdominal discomfort but no fever. He was started on moxifloxacin one week ago to treat pneumonia.

Allergies: Penicillin (anaphylaxis)

Medications: Aspirin 81 mg tablet (OTC) 1 po daily; lisinopril 20 mg tablet 1 po daily; amlodipine 10 mg tablet 1 po daily; moxifloxacin 400 mg tablet 1 po daily for 10 days

Physical Exam/Other Studies:

Wt 192 lb Ht 70 in T 99.1°F BP 138/80 HR 70 RR 14

O_2 sat 98%

Physical exam reveals hyperactive bowel sounds.

SCr 1.1 WBC 7.6

Stool sample is positive for *Clostridium difficile* toxin.

The patient is diagnosed with mild-moderate *Clostridium difficile*-associated diarrhea.

What antibiotic should he receive to treat this infection?

Metronidazole	Nitroimidazole (no other agents)
Mechanism of Action	Interferes with DNA, resulting in inhibition of protein synthesis and cell death
***Contraindications*/ Precautions**	*Hypersensitivity to metronidazole, use during the first trimester of pregnancy*/Patients with seizure disorder or CNS disease, heart failure, and hepatic impairment
Adverse Effects	Urticaria, very dark urine, headache; Rarely: paresthesias, peripheral neuropathy, ataxia, seizure, aseptic meningitis
Drug Interactions	Disulfiram-like reaction can occur when using alcohol during and within 48 hours after use of metronidazole; may increase the effects of warfarin and phenytoin
Monitoring	Follow culture and sensitivity information to direct therapy.
Case Notes	For the treatment of an initial episode of mild-moderate *Clostridium difficile*-associated diarrhea, metronidazole 500 mg 1 tablet po three times daily for 10-14 days is the treatment of choice according to the 2010 SHEA/IDSA *Clostridium difficile* Guidelines. If the patient has a recurrence after this initial treatment, a repeat course of metronidazole would be appropriate. For more severe episodes, or for multiple recurrences, oral vancomycin should be used. The use of loperamide or any other anti diarrheal agent in patients with *Clostridium difficile* associated diarrhea is not recommended. Patients receiving therapy with metronidazole, orally or vaginally, should always be warned about the potential for a disulfiram-like reaction when using alcohol while on metronidazole and for 48 hours after use. Metronidazole may also be used to treat a variety of anaerobic infections. It is also available as a vaginal preparation that can be used in the treatment of bacterial vaginosis.

A 46-year-old woman has been treated with levofloxacin 250 mg tablet 1 po daily for a presumed urinary tract infection. Three days after completing the levofloxacin, she continues to complain of painful urination, urinary urgency, and urinary frequency. She denies any fever, chills, vomiting, or back pain. The patient was recently discharged from a three-week hospitalization following complications from a surgical procedure.

Allergies: Sulfa (rash)

Medications: Aspirin 81 mg tablet (OTC) 1 po daily, lisinopril 20 mg tablet 1 po daily, and amlodipine 10 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 165 lb Ht 65 in T 99.1°F BP 138/80 HR 70 RR 14 O_2 sat 98%

Physical exam reveals no costovertebral angle tenderness, no vaginal discharge or lesions, and mild suprapubic tenderness.

SCr 0.7

Urine culture is positive for vancomycin- and ampicillin/aminoglycoside-resistant *Enterococcus faecalis.*

The patient cannot afford to purchase linezolid to treat this infection.

What other alternative is available to treat this infection?

Nitrofurantoin	Nitrofuran (no other agents)
Mechanism of Action	Nitrofurantoin works by inhibition of several bacterial enzyme systems, interfering with metabolism and potentially cell-wall synthesis.
***Contraindications*/ Precautions**	*Renal dysfunction including anuria, oliguria, significantly increased SCr or creatinine clearance less than 60 mL/min; infants less than 1 month, pregnancy at term or during labor and delivery, history of cholestatic jaundice or hepatic impairment with previous use of nitrofurantoin/*Patients with G6PD deficiency, elderly patients
Adverse Effects	Nausea, vomiting, hypersensitivity, peripheral neuropathy; Rarely: pulmonary reactions (with chronic use), hepatotoxicity
Drug Interactions	No pertinent drug interactions identified
Monitoring	Follow culture and sensitivity information to direct therapy; monitor CBC, liver function; watch for signs and symptoms of pulmonary reactions and neuropathies
Case Notes	Nitrofurantoin is an inexpensive option for the treatment of VRE urinary tract infections. It can also be used first-line as a choice for uncomplicated urinary tract infection (typically caused by *Escherichia coli*). A patient's renal function must be evaluated to determine if the estimated creatinine clearance is greater than 60 mL/min as it does not achieve adequate urinary concentrations in those with renal insufficiency. Nitrofurantoin is not an effective option for the treatment of infections outside of the urinary tract. It is available in two forms, macrocrystals and monohydrate/macrocrystals. The macrocrystals must be given four times daily, while the monohydrate/macrocrystal form is dosed twice daily.

A 48-year-old woman with a history of leukemia has been hospitalized for a prolonged neutropenia following her chemotherapy treatment. Her hospital course has been complicated by several episodes of neutropenic fever and a diagnosis of invasive pulmonary aspergillosis. You are asked to review her anti-infective regimen below.

Allergies: NKDA

Medications: Piperacillin/tazobactam injection 4.5 g intravenously every six hours; levofloxacin injection 750 mg intravenously once daily; vancomycin injection 1,000 mg intravenously every 12 hours; amphotericin B deoxycholate injection 370 mg intravenously once daily

Physical Exam/Other Studies:

Wt 162 lb Ht 63 in T 100.6°F BP 120/76 HR 91 RR 16 O_2 sat 98%
Na 132 K 2.9 Mg 0.8 SCr 5.4 BUN 32

Which of her anti-infective medications may be contributing to her electrolyte abnormalities?

Amphotericin B Deoxycholate	Polyene antifungal (nystatin, amphotericin B deoxycholate, amphotericin B lipid complex, liposomal amphotericin B, amphotericin B colloidal dispersion)
Mechanism of Action	Alters cell membrane permeability by binding to ergosterol; this causes leakage of cell components and cell death.
***Contraindications*/ Precautions**	*Hypersensitivity to amphotericin or any component of the formulation*/Errors due to multiple products; use only in progressive/life-threatening infections; nephrotoxicity, anaphylaxis, infusion-related reactions, leukoencephalopathy; use with caution in renal impairment and in patients receiving leukocyte transfusions; if therapy is stopped for seven days or more, restart at a low dose
Adverse Effects	Hypotension, tachypnea, fever, chills, headache, malaise, hypokalemia, hypomagnesemia, anorexia, nausea, vomiting, diarrhea, heartburn, cramping, pain at injection site, generalized pain, decreased renal function
Drug Interactions	Use with caution with other agents that are nephrotoxic or those that cause hypokalemia; azole antifungal agents may diminish the effects of amphotericin; amphotericin may diminish the effects of *Saccharomyces boulardii.*
Monitoring	Renal function, electrolytes, liver function, temperature, PT/PTT, CBC, input and output, and sign/symptoms of hypokalemia
Case Notes	Amphotericin B deoxycholate is most likely causing this patient to have increased creatinine and decreased potassium and magnesium. The amphotericin products are the most broad-spectrum of the antifungal agents available, but they are some of the most toxic. The lipid preparations were developed to overcome the nephrotoxicity associated with the deoxycholate formulation. The efficacy of the products is very similar. Infusion-related reactions are common, and slowing the infusion rate may help.

A 25-year-old woman presents to the hospital unresponsive after being found by her sister. According to her sister, she had been complaining of right-sided abdominal pain for about one week. She has a history of diabetes mellitus Type 1, which is poorly controlled, chronic kidney disease, hypertension, and hyperlipidemia. She was recently hospitalized for a right renal abscess with the placement of a ureteral stent.

Allergies: NKDA

Medications: Insulin glargine injection 25 units subcutaneously once daily at bedtime; insulin lispro injection 8 units subcutaneously three times daily before meals; lisinopril 20 mg tablet 1 po once daily; aspirin 81 mg tablet (OTC) 1 po once daily; atorvastatin 40 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 130 lb Ht 64.2 in T 97.2°F BP 63/29 HR 57 RR 14 O_2 sat 78%

SCr 3.1 CO_2 5 Glu 1314 WBC 15.1

Urine culture: >100,000 *E coli* susceptibilities pending

Blood culture: *Candida glabrata*

The patient was admitted to the intensive care unit and started on the hospital's diabetic ketoacidosis protocol with an insulin drip and intravenous fluids. She was also placed on norepinephrine for blood pressure support. Antibiotic therapy was initiated with piperacillin/tazobactam, levofloxacin, and vancomycin.

What class of antifungal agents would be the best to initiate in this patient for the treatment of her *Candida glabrata* bloodstream infection?

Echinocandin	Anidulafungin, caspofungin, micafungin
Mechanism of Action	Inhibits the synthesis of beta-(1,3)-D-glucan, an essential component of fungal cell walls
***Contraindications*/ Precautions**	*Hypersensitivity*/Caspofungin: hepatic impairment; micafungin: anaphylaxis, hemolytic anemia, hemoglobinuria, renal impairment, hepatic failure; anidulafungin: hepatic effects, histamine-mediated reactions, safety and efficacy have not been established in pediatrics or neutropenic patients or in endocarditis, osteomyelitis, or meningitis
Adverse Effects	Nausea, diarrhea, vomiting, hypotension, edema, fever, chills, headache, hypokalemia, increased LFTs
Drug Interactions	Echinocandins may decrease the effects of *Saccharomyces boulardii*; conivaptan may increase micafungin concentrations; cyclosporine may increase caspofungin concentrations; rifampin may decrease caspofungin concentrations; caspofungin may decrease tacrolimus concentrations.
Monitoring	Liver function
Case Notes	The echinocandins would be a good choice in this patient who has a *Candida glabrata* bloodstream infection in the intensive care unit. The azole antifungals may have decreased susceptibility to this fungus and may not be the best choice until susceptibilities are known. The echinocandins also have activity against *Aspergillus* species and other *Candida* species with the exception of *C parapsilosis* for which they have variable activity. These agents have low urine concentrations and are not very useful for urinary infections. However, they are becoming more useful in the treatment of systemic fungal infections due to their lack of systemic toxicities compared to the other antifungal agents. The most common adverse reaction is an infusion-related reaction that is histamine-mediated. This can be relieved by slowing the rate of infusion or premedicating with an antihistamine such as diphenhydramine.

A 21-year-old woman presents to the pharmacy counter requesting help for vaginal itching. Upon further questioning, she reveals that a few days ago, she began to experience mild vaginal itching that has since progressed to more intense itching and a burning sensation. Additionally, she reports a curd-like white vaginal discharge that is nonodorous. She reports that this is the fifth time in the past year that she has experienced these symptoms. Each time, she has managed to treat the problem with over-the-counter clotrimazole vaginal tablets. However, she is concerned that this treatment may not be working and her physician suggested that she ask the pharmacist to help her choose a different treatment. Her past medical history is significant for diabetes mellitus Type 1 and frequent methicillin-resistant *Staphylococcus aureus* skin infections requiring repeated courses of antibiotics.

Allergies: Sulfa (rash)

Medications: Insulin lispro injection administered via an insulin pump

Physical Exam/Other Studies:

Wt 132 lb Ht 62 in T 98.6°F BP 125/76 HR 71 RR 16 O_2 sat 98%
Glu (fasting) 100

After a discussion with the patient, the pharmacist recommends treatment with miconazole vaginal suppositories for 14 days.

Following treatment, what would be the best agent to use for suppression of these recurrent episodes of *Candida* vaginitis?

Fluconazole	Systemic triazole (fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole)
Mechanism of Action	Decreases ergosterol synthesis by interfering with fungal cytochrome P450 activity (blocking the demethylation of lanosterol) and inhibiting cell membrane formation
***Contraindications*/ Precautions**	*Hypersensitivity to fluconazole, other azoles, or any component of the formulation, concomitant use with cisapride*/Skin reactions, arrhythmias, hepatotoxicity, use with caution in renal impairment and hepatic impairment
Adverse Effects	Headache, rash, nausea, and rarely QT prolongation and hepatitis
Drug Interactions	Inhibitor of CYP2C9, CYP2C19, and CYP3A4
Monitoring	Liver function, renal function, and potassium
Case Notes	Fluconazole is the triazole antifungal agent of first choice for the treatment of oropharyngeal, esophageal, and vaginal candidiasis. It is well absorbed and has >90% bioavailability. The normal adult dose ranges from 150 mg for vulvovaginal infections up to 800 mg for invasive fungal infections. Fluconazole also has good activity against *Cryptococcus* and is often used in treating those infections. It does not have activity against *Aspergillus* species or *C krusei*, and has variable activity against *C glabrata*. For the treatment of vaginal candidiasis, both oral and topical regimens achieve similar efficacy. However, for the suppression of recurrent episodes, the most convenient regimen is fluconazole 150 mg orally once weekly for six weeks.

A 44-year-old man presents to the pharmacy counter with a prescription for simvastatin 40 mg tablets. His past medical history is significant for poorly controlled diabetes mellitus Type 2, blindness secondary to retinopathy, chronic renal insufficiency, neuropathy, and pulmonary sporotrichosis, which was diagnosed about nine months ago.

Allergies: NKDA

Medications: Gabapentin 300 mg tablet 1 po three times daily; insulin glargine injection 40 units subcutaneously at bedtime; insulin aspart injection 8 units subcutaneously before each meal; citalopram 20 mg tablet 1 po once daily; itraconazole 10 mg/mL 300 mg twice daily; enalapril 10 mg tablets 1 po twice daily

Physical Exam/Other Studies:

Wt 182 lb Ht 69 in T 98.6°F BP 155/76 HR 91 RR 16 O_2 sat 98%

As the pharmacist is filling the prescription for simvastatin, a drug interaction warning appears on the computer screen.

Simvastatin is contraindicated with which of the patient's current medications?

Itraconazole	Systemic triazole (fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole)
Mechanism of Action	Decreases ergosterol synthesis by interfering with fungal cytochrome P450 activity (blocking the demethylation of lanosterol) and inhibiting cell membrane formation
***Contraindications*/ Precautions**	*Hypersensitivity to itraconazole, other azoles, or any component of the formulation; concomitant use with cisapride, dofetilide, ergot derivatives, levomethadyl, lovastatin, midazolam (oral), nisoldipine, pimozide, quinidine, simvastatin, triazolam; treatment of onychomycosis in patients with ventricular dysfunction or pregnancy; patients with heart failure or a history of heart failure*/Heart failure; high potential for interactions, hearing loss, hepatotoxicity, neuropathy, pharmacokinetics may differ in cystic fibrosis patients, use with caution in renal impairment
Adverse Effects	Nausea, diarrhea, edema, rash
Drug Interactions	Substrate of CYP3A4, inhibitor of CYP3A4 and P-glycoprotein
Monitoring	Liver function, renal function, and serum drug concentrations in patients on oral therapy due to erratic bioavailability with the capsule formulation
Case Notes	Itraconazole is used for the treatment of fungal infections including blastomycosis and histoplasmosis. It is also used in aspergillosis for patients who cannot tolerate amphotericin B and for onychomycosis in nonimmunocompromised patients. The oral solution can be used for treating oral and esophageal candidiasis, but the capsule should not be used due to differences in mucosal exposure. Itraconazole requires gastric acidity for absorption, and the capsule is better absorbed with food, while the solution is best absorbed on an empty stomach. For patients taking gastric acid suppressants, cola drinks may improve the absorption of the capsules. Due to the significant amount of drug interactions that may occur, diligence must be used when filling prescriptions for patients on itraconazole.

A 48-year-old woman with a history of leukemia has been hospitalized for a prolonged neutropenia following her chemotherapy treatment. Her hospital course has been complicated by several episodes of neutropenic fever and a diagnosis of invasive pulmonary aspergillosis. She has been treated with amphotericin B deoxycholate injection, but has had significant electrolyte abnormalities that have not been manageable.

Allergies: NKDA

Medications: Piperacillin/tazobactam injection 4.5 g intravenously every six hours; levofloxacin injection 750 mg intravenously once daily; vancomycin injection 1,000 mg intravenously every 12 hours; amphotericin B deoxycholate injection 370 mg intravenously once daily

Physical Exam/Other Studies:

Wt 162 lb Ht 63 in T 100.6°F BP 120/76 HR 91 RR 16 O_2 sat 98%
Na 132 K 2.9 Mg 0.8 SCr 1.4 BUN 32

What antifungal could be used in place of the amphotericin B to treat the invasive pulmonary aspergillosis?

Voriconazole	Systemic triazole (fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole)
Mechanism of Action	Decreases ergosterol synthesis by interfering with fungal cytochrome P450 activity (blocking the demethylation of lanosterol) and inhibiting cell membrane formation
***Contraindications*/ Precautions**	*Hypersensitivity to voriconazole or any component of the formulation, coadministration with CYP3A4 substrates that may lead to QTc prolongation, coadministration with barbiturates (long-acting), carbamazepine, efavirenz (standard dosing), ergot derivatives, rifampin, rifabutin, ritonavir (≥800 mg/day), sirolimus, St John's wort*/ Arrhythmias/QT prolongation, dermatologic reactions, hallucinations, ocular effects, use with caution in hepatic impairment, pancreatitis, renal impairment, avoid injectable form in renal impairment, lactose allergy (tablets), sucrose allergy (suspension)
Adverse Effects	Hallucinations, visual changes, increased creatinine, phototoxicity
Drug Interactions	Substrate of CYP2C9, CYP2C19, CYP3A4; inhibitor of CYP2C9, CYP2C19, and CYP3A4
Monitoring	Hepatic function, renal function, electrolytes, visual function, trough levels in patients failing therapy or with signs of toxicity, pancreatic function, total body skin examination
Case Notes	Voriconazole is the triazole antifungal approved for the primary treatment of invasive aspergillosis. It is available as a tablet, suspension, or intravenous formulation, and would be an alternative to amphotericin for this patient. Due to its significant effects on the CYP system, all patient profiles should be reviewed for drug interactions prior to initiating therapy. The dose in the treatment of aspergillosis is 6 mg/kg IV every 12 hours for two doses followed by 4 mg/kg every 12 hours. Patients with a Clcr < 50 ml/min may accumulate the IV vehicle (cyclodextrin) and should use the oral route for their therapy. The two unique adverse effects to voriconazole are the visual disturbances and the cutaneous phototoxicity. Patients may experience bright lights, color changes, or wavy lines in their vision, which typically resolves with continued treatment. The phototoxicity is not preventable with sunscreen but is reversible upon discontinuation of therapy.

A 26-year-old man with active tuberculosis presents to the pharmacy counter asking for help finding vitamin B_6 tablets (pyridoxine). He was recently started on a four-drug regimen for his tuberculosis infection, and his physician told him that the needed to take vitamin B_6 tablets daily. He is willing to take these tablets, but he wonders why he needs to do so. His past medical history is unremarkable. He smokes one pack of cigarettes daily and drinks one to two beers every evening.

Allergies: NKDA

Medications: Ethambutol 400 mg tablet 3 po once daily; isoniazid 300 mg tablet 1 po once daily; pyrazinamide 500 mg tablet 3 po once daily; rifampin 300 mg capsule 2 po once daily

Physical Exam/Other Studies:

Wt 154 lb Ht 67 in T 98.4°F BP 125/76 HR 68 RR 16

The pyridoxine supplementation is being recommended to prevent a side effect of which of his antituberculosis medications?

Isoniazid	Antitubercular agent (capreomycin, cycloserine, ethambutol, ethionamide, isoniazid, pyrazinamide, rifabutin, rifampin, rifapentine, streptomycin)
Mechanism of Action	The exact mechanism is unknown, but it may work through inhibition of mycolic acid synthesis leading to disruption of the bacterial cell wall.
***Contraindications*/ Precautions**	*Hypersensitivity to isoniazid or any component of the formulation, acute liver disease, previous history of isoniazid-induced hepatotoxicity or previous severe reaction to isoniazid therapy*/ Hepatitis (boxed warning), peripheral neuropathies, use with caution in hepatic or renal failure
Adverse Effects	Increased LFTs, hepatitis, peripheral neuropathy, CNS effects, lupus-like syndrome
Drug Interactions	Substrate of CYP2E1; inhibitor of: CYP2A6, CYP2C19, CYP2D6, CYP2E1, and CYP3A4
Monitoring	LFTs, bilirubin, sputum cultures, physical exam (brief) for adverse effects
Case Notes	This patient is being asked to take pyridoxine to help prevent peripheral neuropathy while using isoniazid. Isoniazid is one of the most common agents used in the treatment of tuberculosis. It is one of the first-line agents in the preferred initial four-drug regimen for the treatment of patients with tuberculosis caused by drug-susceptible organisms. The adult dose is 5 mg/kg (maximum 300 mg) daily or 15 mg/kg (900 mg maximum) once, twice, or three times weekly. One of the major warnings associated with this agent is hepatotoxicity. Although rare, hepatotoxicity can occur in any patient on isoniazid. Risk factors for hepatotoxicity include age, liver disease, alcohol use, and pregnancy. Pregnant women, alcoholics, children, and malnourished individuals are at an increased risk for neurotoxicity. Due to the concerns for hepatotoxicity and the possibility for major drug interactions, patients should be monitored closely.

A 32-year-old man presents to the anticoagulation clinic for a follow-up appointment. He has been on warfarin for the past year due to multiple episodes of deep vein thrombosis related to a hypercoagulable disorder. Two weeks ago, he was hospitalized and was diagnosed with tuberculosis. On his last visit to the anticoagulation clinic, six weeks ago, his INR was 2.6. Besides his antituberculosis medications, he reports no other changes to his medication regimen or diet.

Allergies: NKDA

Medications: Ethambutol 400 mg tablet 3 po once daily; isoniazid 300 mg tablet 1 po once daily; pyridoxine 25 mg tablet 1 po once daily; pyrazinamide 500 mg tablet 3 po once daily; rifampin 300 mg capsule 2 po once daily; warfarin 7.5 mg po once daily

Physical Exam/Other Studies:

Wt 154 lb Ht 67 in T 98.4°F BP 125/76 HR 68 RR 16

INR 0.86

Which of his antituberculosis medications has likely contributed to his subtherapeutic INR?

Rifampin	Antitubercular agent (capreomycin, cycloserine, ethambutol, ethionamide, isoniazid, pyrazinamide, rifabutin, rifampin, rifapentine, streptomycin)
Mechanism of Action	Blocks RNA transcription by inhibition of bacterial RNA synthesis through binding to the beta subunit of DNA-dependent RNA polymerase
Contraindications/ Precautions	*Hypersensitivity to rifampin, any rifamycins, or any component of the formulation, do not use with amprenavir or saquinavir/ritonavir (and possibly other protease inhibitors)*/Flu-like syndrome, hematologic effects, hyperbilirubinemia, prolonged use may result in superinfection, use with caution in patients with alcoholism, hepatic impairment, or porphyria, do not wear soft contact lenses during treatment
Adverse Effects	Rash, fever, gastrointestinal distress, flu-like syndrome, staining of contact lenses, red/orange discoloration of urine, feces, saliva, sweat, tears, and CSF
Drug Interactions	Substrate of P-glycoprotein; inducer of CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP3A4, and P-glycoprotein
Monitoring	LFTs, bilirubin, CBC, hepatic/mental status, sputum cultures, chest x-ray
Case Notes	Rifampin is one of the most common agents used in the treatment of tuberculosis. It may also be used for prophylaxis against meningococci and for the treatment of staphylococcal infections in combination with other agents. It is one of the first-line agents in the preferred initial four-drug regimen for the treatment of patients with tuberculosis caused by drug-susceptible organisms. The adult dose is 10 mg/kg (max 600 mg) once daily, twice weekly, or three times weekly. There are a number of drug interactions described with rifampin. Many of these interactions are very serious, resulting in a reduction in the therapeutic level of other agents, such as warfarin in this patient case. Any inhibition that occurs due to isoniazid use is overcome by the strong induction caused by rifampin. Drug interaction screening should always be conducted.

A 26-year-old man with active tuberculosis presents to the pharmacy counter requesting help with over-the-counter medications for pain. Upon further questioning, he reveals that he has pain in his left big toe that has increasingly gotten worse over the past two weeks. In addition, the toe is tender and red. Before providing him with a recommendation for treating his pain, you review his medications.

Allergies: NKDA

Medications: Ethambutol 400 mg tablet 3 po once daily; isoniazid 300 mg tablet 1 po once daily; pyridoxine 25 mg tablet 1 po once daily; pyrazinamide 500 mg tablet 3 po once daily; rifampin 300 mg capsule 2 po once daily

Physical Exam/Other Studies:

Wt 154 lb Ht 67 in T 98.4°F BP 125/76 HR 68 RR 16

Physical exam is positive for a tender and red left great toe.

Uric acid 12 mg/dL

Which of the patient's medications is likely causing his toe pain?

Pyrazinamide	Antitubercular agent (capreomycin, cycloserine, ethambutol, ethionamide, isoniazid, pyrazinamide, rifabutin, rifampin, rifapentine, streptomycin)
Mechanism of Action	Conversion to pyrazinoic acid occurs in susceptible strains of *Mycobacterium*. This leads to a decreased pH of the environment, but the exact mechanism of action has not been determined.
***Contraindications*/ Precautions**	*Hypersensitivity to pyrazinamide or any component of the formulation, acute gout, severe hepatic damage*/Hepatotoxicity, use with caution in patients with diabetes, gout, porphyria, renal failure, and with other hepatotoxic agents
Adverse Effects	Malaise, anorexia, nausea, vomiting, arthralgias, myalgias, and rarely gout
Drug Interactions	Cyclosporine concentrations may be either increased or decreased; pyrazinamide may enhance the hepatotoxicity of rifampin when used together longer than two months
Monitoring	LFTs, serum uric acid, sputum culture, and chest x-ray
Case Notes	Pyrazinamide is one of the first-line agents in the preferred initial four-drug regimen for the treatment of patients with tuberculosis caused by drug-susceptible organisms. Pyrazinamide is typically dosed based on patient weight. Hepatotoxicity is usually the major limiting adverse reaction. This is more likely in patients with underlying liver disease and with prolonged durations of treatment. It is likely that the patient in the case is experiencing a rare side effect of gout related to pyrazinamide. Both pyrazinamide and ethambutol are typically discontinued after the first two months of treatment. Ethambutol interferes with RNA synthesis and is also dosed based on patient weight. The most notable information regarding ethambutol is the need for patients to have a visual acuity test and color discrimination test at baseline due to the possibility of optic neuritis.

A 40-year-old man presents to HIV clinic for assessment of his most recent laboratory results. He has been coming to this clinic for HIV treatment for the past 10 years and has recently experienced an increasing viral load. His most recent regimen has been effective for five of the last 10 years since his diagnosis. The HIV treatment team is considering initiation of a new agent to treat his HIV and reduce his viral load to undetectable (<50 copies/mL). In addition to HIV, he has been diagnosed with dyslipidemia.

Allergies: NKDA

Medications: Efavirenz 600 mg tablet 1 po at bedtime on an empty stomach; abacavir 300 mg tablet 2 po daily; lamivudine 300 mg tablet 2 po daily; atorvastatin 10 mg tablet 1 po daily; fish oil 1,000 mg capsule (OTC) 1 po three times daily; aspirin 81 mg tablet (OTC) 1 po every morning

Physical Exam/Other Studies:

Wt 130 lb Ht 64 in T 96.9°F BP 122/76 HR 68 RR 18

Physical exam reveals no pertinent findings.

Na 137 K 3.7 Cl 102 Clcr 74 SCr 1.1 VL 1045 CD4 348

This patient has a viral load that is not suppressed with his current therapy. Before a medication can be selected, all options must be explored. No coreceptor tropism assay tests have been run on this patient.

Which antiretroviral therapy requires coreceptor tropism assay to be performed before initiation?

A. maraviroc
B. enfuvirtide
C. raltegravir
D. tipranavir

Maraviroc	CCR5 inhibitor
Mechanism of Action	Prevents HIV entry into target cells by binding to the CCR5 receptor
***Contraindications*/ Precautions**	*Patients with severe renal impairment (Clcr <30 mL/min) or end-stage renal disease who are taking potent CYP3A4 inhibitors or inducers*/Hepatotoxicity, immune reconstitution syndrome, infections, postural hypotension, cardiovascular disease, hepatic/renal impairment
Adverse Effects	Abdominal pain, cough, dizziness, musculoskeletal symptoms, pyrexia, rash, upper respiratory tract infections, hepatotoxicity, orthostatic hypotension
Drug Interactions	Substrate of the CYP3A enzymes and P-glycoprotein; therefore when in combination with inhibitors and inducers of CYP3A enzymes, dose adjustments should be made. Dasatinib, deferasirox, and St John's wort should be avoided due to decreased serum concentration of maraviroc.
Monitoring	Viral load, CD4 count, transaminases; signs/symptoms of infection, hepatitis, and/or allergic reaction; postural hypotension; tropism testing (prior to initiation)
Case Notes	Maraviroc is only effective in patients with HIV strands that attack the CCR5 receptors. This medication is ineffective in patients with viruses that attack the CXCR4 receptor only. Dosing for patients 16 and older is 300 mg po twice daily. When given with strong CYP3A inducers (efavirenz, etravirine, etc.), dose should be increased to 600 mg po twice daily. When given with strong CYP3A inhibitors (protease inhibitors except tipranavir/ritonavir), dose should be decreased to 150 mg po twice daily. Trough concentrations should be >50 ng/mL in treatment-experienced patients with resistant HIV-1 strains only.

A 53-year-old African-American man presents to your internal medicine clinic for consultation on starting antiretroviral therapy today. He has recently been diagnosed with HIV and is interested in starting medications. He has been diagnosed with HTN, seasonal allergies, and genital herpes in the past. Currently, he is taking valacyclovir daily for genital herpes preventative therapy. He is a heterosexual male and reports having multiple sexual partners in his lifetime. He reports he contracted HIV through risky sexual behavior.

Allergies: Sulfa (facial swelling), codeine (rash)

Medications: Enalapril/hydrochlorothiazide 10/25 mg tablet 1 po every morning; loratadine 10 mg tablet (OTC) 1 po every morning; valacyclovir 1,000 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 150 lb Ht 69 in T 98.9°F BP 126/80 HR 86 RR 17

Na 139 K 3.8 Cl 98 ALT 33 AST 38 SCr 1.2 CD4 340 VL 480,000

Because this patient is treatment naïve, he is going to be started on a regimen containing two nucleoside reverse transcriptase inhibitors and a non-nucleoside reverse transcriptase inhibitor. Tenofovir and emtricitabine were recommended.

What additional antiretroviral therapy should be added to this patient's regimen?

Efavirenz	Non-nucleoside reverse transcriptase inhibitor (delavirdine, nevirapine, etravirine, efavirenz)
Mechanism of Action	Binds to reverse transcriptase and consequently blocks the RNA-dependent and DNA-dependent DNA polymerase activities including HIV-1 replication. It does not require intracellular phosphorylation for antiviral activity.
***Contraindications*/ Precautions**	*Hypersensitivity, concurrent use of medications metabolized by CYP3A4 isoenzyme/*CNS depression, fat redistribution, hypercholesterolemia, psychiatric effects, rash, hepatic impairment, seizure disorder
Adverse Effects	Dizziness, fever, depression, insomnia, anxiety, vivid dreams, pain, headache, rash, increases in cholesterol, diarrhea, nausea, vomiting, cough, hyperglycemia, elevated liver enzymes, headache, teratogenicity
Drug Interactions	Major substrate of CYP2B6, 3A4; moderate inhibitor of CYP2C9, 2C19, 3A4; strong inducer of CYP3A4
Monitoring	Monitor serum transaminases (discontinuation of treatment should be considered for persistent elevations greater than five times the upper limit of normal), cholesterol, and triglycerides
Case Notes	Efavirenz is the best additional medication for this patient's regimen. This regimen helps reduce pill burden and improve compliance due to an available combination product of efavirenz, tenofovir, and emtricitabine. Efavirenz has been reported to cause a false-positive cannabinoid screen and is also teratogenic in monkeys; therefore, it is not recommended in females of childbearing age. Although most NNRTIs can be administered with or without food, efavirenz must be administered on an empty stomach. Nevirapine is not recommended in treatment-naïve patients with high CD4 counts (females >250, males >400) because of hepatotoxicity risk. Efavirenz is dosed 600 mg po daily and is taken at bedtime because of potential vivid dreams.

A 48-year-old woman presents to the internal medicine clinic for evaluation of HIV labs and therapy. She has had HIV for 15 years and an undetectable viral load (<50 copies/mL) until approximately one year ago. She was changed from her initial regimen of two NRTIs and one NNRTI to a regimen of a PI boosted with ritonavir and two NRTIs not previously taken. She has since failed this regimen, and resistance testing shows she is resistant to almost all NRTI and NNRTI drugs. She has a past medical history of HIV, dyslipidemia, and hypertension.

Allergies: Codeine (rash), ibuprofen (rash), hydromorphone (airway swelling)

Medications: Tipranavir 250 mg capsule 2 po twice daily; ritonavir 100 mg capsule 2 po twice daily; emtricitabine/tenofovir 200/300 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; lisinopril 20 mg tablet 1 po every morning; atorvastatin 10 mg tablet 1 po at bedtime; trimethoprim/sulfamethoxazole 800/160 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 140 lb Ht 63 in T 98.1°F BP 130/78 HR 72 RR 18

Physical exam reveals no pertinent findings.

Na 142 K 4.5 Cl 105 SCr 1.1 CD4 188 VL 50,000

Because this patient is in virologic failure, her regimen must be adjusted. According to her history, she still has options to which she is not yet resistant.

What medication is indicated for treatment of an HIV patient in virologic failure?

Enfuvirtide (T20)	Fusion inhibitor
Mechanism of Action	Inhibits the fusion of HIV-1 virus with CD4 cells by blocking the conformational change in gp41 required for membrane fusion and entry into CD4 cells
***Contraindications*/ Precautions**	*Hypersensitivity*/Immune reconstitution syndrome, injection site reactions, pneumonia, bleeding disorders, pediatrics (<6 years of age)
Adverse Effects	Local injection site reactions in almost 100% of patients, increased bacterial pneumonia, hypersensitivity reactions (rechallenge is not recommended), fatigue, diarrhea, nausea, weight loss, abdominal pain, eosinophilia, increased transaminases
Drug Interactions	May increase serum concentration of protease inhibitors
Monitoring	Use caution and monitor closely for symptoms of pneumonia with history of IV drug use, smoking, or lung disease. Assess therapeutic response (CD4 level and viral load) and adverse reactions on a regular basis throughout therapy.
Case Notes	This medication is indicated for patients experiencing virologic failure. It is not appropriate for treatment-naïve patients, nor should it be used as monotherapy. There are no data to support its use in treatment-naïve patients. Dosing is 90 mg (1 mL) injected subcutaneously twice daily. Once reconstituted, injection should be refrigerated and given within 24 hours. Teach patient or caregiver proper use (eg, reconstitution, injection procedure, needle/syringe disposal, and proper timing of medications). Teach patient possible side effects/appropriate interventions and adverse symptoms to report (eg, hypersensitivity reactions, injection site infection). No dose adjustment is required in patients with renal or hepatic impairment.

A 35-year-old Caucasian woman presented to the hospital one day ago with a diagnosis of pneumonia. She reported a history of having many sexual partners with lack of consistent protection from sexually transmitted diseases. Upon admission, she consented to a test for HIV, which was confirmed today as being positive. After discussion with the physician about antiretroviral treatment, she has decided she would like to start therapy for her HIV. She reports she has had a heart attack in the past but only takes aspirin and pravastatin regularly.

Allergies: NKDA

Medications: Aspirin 81 mg tablet (OTC) 1 po daily; pravastatin 40 mg tablet 1 po at bedtime

Physical Exam/Other Studies:

Wt 110 lb Ht 62 in T 101.2°F BP 118/78 HR 20 RR 20 O_2 sat 98%

Na 136 K 3.8 Cl 101 SCr 0.9

Pneumocystis stain (+)

This patient needs to begin a multi drug regimen for her HIV/AIDS. The regimen will consist of a double NRTI backbone (emtricitabine and tenofovir) and one other agent.

Which medication is an appropriate first-line drug to add to this treatment-naïve patient's regimen?

A. enfuvirtide C. efavirenz

B. raltegravir D. zidovudine

Raltegravir	Integrase inhibitor
Mechanism of Action	Inhibits the catalytic activity of integrase, thus preventing integration of the proviral gene into human DNA
***Contraindications*/ Precautions**	Immune reconstitution syndrome, myopathy
Adverse Effects	Nausea, headache, diarrhea, pyrexia, hypertension, fatigue, dizziness, rash, pruritus, folliculitis, abdominal pain, insomnia, and elevations in cholesterol, glucose, triglycerides, transaminases, bilirubin, CPK, and creatinine
Drug Interactions	Serum concentration may be decreased by rifampin, tipranavir, efavirenz, and St John's wort; proton pump inhibitors may increase the serum concentration of raltegravir
Monitoring	Viral load, CD4 count, lipid profile
Case Notes	Raltegravir is the best option for this patient based on its minimal impact on lipids. This patient has had a CHD event in the past; therefore, lipids must be closely monitored. Enfuvirtide is not an appropriate choice because it is only indicated for treatment-experienced patients. Efavirenz is not appropriate because of its teratogenic potential. Zidovudine is not a good choice because it is an NRTI like tenofovir and emtricitabine. When paired with a double NRTI backbone (specifically tenofovir and emtricitabine), this regimen is appropriate for treatment-naïve patients. Raltegravir is dosed 400 mg po bid and can be taken without regard to meals. This medication should be avoided in severe hepatic insufficiency. This medication is also appropriate for treatment-experienced patients.

A 31-year-old man presents to your internal medicine clinic for initial assessment of his HIV medications. He has been referred to you by his current primary care physician after learning he had HIV three months ago. He was started on a regimen consisting of efavirenz and tenofovir and needs your help in assessing the appropriateness of this current therapy. His past medical history is significant for hypertension, dyslipidemia, and chronic alcoholism. He is a homosexual male with a steady partner who is also HIV positive. He has a mother with a history of heart disease and had a stroke at age 60. His father has diabetes.

Allergies: NKDA

Medications: Efavirenz 600 mg tablet 1 po at bedtime; tenofovir 300 mg tablet 1 po at bedtime; atorvastatin 10 mg tablet 1 po at bedtime; hydrochlorothiazide 25 mg tablet 1 po every morning; aspirin 81 mg tablet (OTC) 1 po every morning; fish oil 1,000 mg capsule (OTC) 1 po three times daily; multivitamin tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 167 lb Ht 68 in T 97.1°F BP 138/78 HR 66 RR 18

Physical exam reveals no pertinent findings.

Na 137 K 4.2 Cl 98 SCr 1.4 Clcr 82 fasting glucose 98 AST 40 ALT 42

TC 198 LDL 121 HDL 45 TG 232 CD4 348 VL 98,000

A medication from what class needs to be added to this patient's regimen to help prevent resistance to the other antiretroviral therapies?

A. nucleoside reverse transcriptase inhibitors (NRTIs)
B. non-nucleoside reverse transcriptase inhibitors (NNRTIs)
C. protease inhibitors (PIs)
D. entry inhibitors

Nucleoside (Nucleotide) Reverse Transcriptase Inhibitor (NRTI)	Abacavir, adefovir, didanosine, emtricitabine, entecavir, lamivudine, stavudine, telbivudine, tenofovir, zidovudine
Mechanism of Action	NRTIs interfere with the HIV viral RNA-dependent DNA polymerase resulting in inhibition of viral replication.
***Contraindications*/ Precautions**	*Hypersensitivity*/Lactic acidosis with hepatomegaly, fat redistribution, pancreatitis, renal impairment, bone marrow suppression, exacerbation of hepatitis B
Adverse Effects	Depends on the individual NRTI; possible distinguishing reactions include peripheral neuropathy, pancreatitis, headache, lipoatrophy, renal toxicity, anemia, neutropenia, myopathy
Drug Interactions	Ganciclovir, valganciclovir, or lamivudine may enhance toxic effects of NRTI; ribavirin may enhance hepatotoxic effect of NRTI; see individual drug references for specific NRTIs; didanosine and stavudine combination should be avoided due to increased risk of peripheral neuropathy, pancreatitis, and lactic acidosis; stavudine and zidovudine combination should be avoided due to antagonism demonstrated *in vitro* and *in vivo*
Monitoring	Amylase, bilirubin, liver enzymes, hematologic parameters, HIV viral load, and CD4 count; signs/symptoms of pancreatitis, HBV DNA, HBeAg and anti-HBe; signs/symptoms of HBV relapse/exacerbation
Case Notes	This patient is currently on one NRTI (tenofovir) and one NNRTI (efavirenz). To complete his regimen, he needs one more NRTI. The preferred regimen is tenofovir + efavirenz + emtricitabine, but other agents may be appropriate depending on the patient. To help reduce pill burden, a combination product exists with these three medications, and is dosed 1 tablet po daily. This regimen should not be used for females of childbearing age, because efavirenz is pregnancy category D. Stavudine should not be used in combination with didanosine due to fatal risk of lactic acidosis in pregnant women. Zidovudine carries a risk of macrocytic anemia.

A 21-year-old woman presents to your internal medicine clinic after being diagnosed with HIV during a recent hospital admission after an overdose. She is an IV drug user and reports most likely contracting the disease through needle sharing. She has no other health conditions at this time. She is currently not sexually active, but does have a history of sex with multiple partners. She has two female roommates that are also IV drug users and reports sharing needles with these women. She was referred to clinic today to begin an antiretroviral regimen and is treatment naïve.

Allergies: NKDA

Medications: No prescription or over-the-counter medications reported, although this patient is a current IV methamphetamine user and reports using approximately three times per day.

Physical Exam/Other Studies:

Wt 120 lb Ht 60 in T 97.9°F BP 148/82 HR 90 RR 18

Na 141 K 4.1 Cl 101 ALT 32 AST 28 SCr 1.0 CD4 220 VL 120,000

HIV status confirmed by an ELISA rapid test and further validated using Western blot

Because this patient has a CD4 count between 201 and 350, she should be offered therapy. After discussing the benefits of treating her HIV now, she decides she would like to start antiretroviral therapy to suppress the viral load and rebuild her CD4 cell count. Because of her age, reproductive potential, and therapy naivety, you decide she should begin on a regimen with two nucleoside reverse transcriptase inhibitors (NRTIs) and another class of medications.

What other class of medications should be used in this patient to help prevent resistance to the NRTIs?

Protease Inhibitor (PI)	Atazanavir, darunavir, fosamprenavir, indinavir, nelfinavir, ritonavir, saquinavir, tipranavir, lopinavir
Mechanism of Action	Binds to the site of HIV-1 protease activity and inhibits cleavage of viral polyprotein precursors into individual functional proteins required for infectious HIV. This results in the formation of immature, noninfectious viral particles.
***Contraindications*/ Precautions**	*Hypersensitivity (such as Stevens-Johnson syndrome, skin eruptions, etc), concurrent cisapride, ergot derivatives, indinavir, irinotecan, lovastatin, midazolam, pimozide, rifampin, simvastatin, St John's wort, or triazolam*/ Elevated bilirubin, fat redistribution, nephrolithiasis, conduction abnormalities, diabetes, hemophilia, hepatic impairment
Adverse Effects	Rash, cholesterol disturbances, gastrointestinal disturbances, increased bilirubin, increased CPK, AV block, peripheral neuropathy, fever, jaundice, myalgias, rhinorrhea, hyperglycemia
Drug Interactions	Strong inhibitor of CYP3A4
Monitoring	Viral load, CD4, serum glucose, liver function tests, bilirubin, drug levels (with certain concomitant medications), ECG monitoring in patients with prolonged PR interval or with concurrent AV nodal blocking drugs
Case Notes	Treatment-naïve HIV patients willing to begin antiretroviral therapy should be on a multidrug regimen to prevent resistance. PIs are a good addition to this regimen because this woman is of childbearing age and should not receive NNRTIs. Protease inhibitors require boosting with ritonavir to prevent resistance to the individual agent. Combination products containing protease inhibitors exist to decrease the pill burden in HIV patients. PIs are usually dosed with food, with few exceptions. Fosamprenavir and amprenavir can be dosed with or without food, but avoid high-fat meals with amprenavir. Indinavir is dosed one hour before or two hours after meals and should be taken with ample water. Saquinavir should be given no more than two hours after meals.

A 27-year-old man presents to your family practice clinic complaining of malaise, fever, nonproductive cough, myalgias, and headache for the past 12 hours. He works in a pharmacy where he is a cashier. He reports he thinks he might have the flu because many of the customers he has interacted with have been complaining of the same "flu-like symptoms" he is experiencing. He has a history of dyslipidemia, and his records indicate he did not receive the influenza vaccine this past fall.

Allergies: Egg (rash, airway obstruction, facial edema)

Medications: Simvastatin 20 mg tablet 1 po at bedtime; fish oil 1,000 mg capsule (OTC) 1 po daily; ibuprofen 200 mg tablet (OTC) 1 po every four to six hours prn muscle pain and/or headaches

Physical Exam/Other Studies:

Wt 210 lb Ht 70 in T 103.0°F BP 138/80 HR 76 RR 16 O_2 sat 99%

Physical exam reveals no signs/symptoms of pneumonia.

Rapid influenza detection test indicates patient is (+) for influenza type B in nasal secretions.

Based on positive identification of influenza type B paired with signs and symptoms, this patient needs treatment for his influenza infection. He is within the 48-hour window for treatment, so the most appropriate medication should be initiated today.

Which medication class should be avoided in this patient for treatment of influenza based on evidence and efficacy?

Adamantanes	Rimantadine, amantadine
Mechanism of Action	Antiviral action: blocks the uncoating of influenza A virus preventing penetration of virus into host; antiparkinsonian action: may be due to its blocking the reuptake of dopamine into presynaptic neurons or by increasing dopamine release from presynaptic fibers
***Contraindications*/ Precautions**	*Hypersensitivity*/CNS depression, impulse control disorders, melanoma, neuroleptic malignant syndrome, suicidal ideation, cardiovascular disease, eczema, glaucoma, hepatic or renal impairment, psychosis, seizure disorder
Adverse Effects	Orthostatic hypotension, peripheral edema, agitation, anxiety, ataxia, confusion, delirium, depression, dizziness, dream abnormality, fatigue, hallucinations, headache, insomnia, irritability, lightheadedness, nervousness, anorexia, constipation, diarrhea, nausea, xerostomia
Drug Interactions	Atypical antipsychotics may diminish effects of dopamine agonists (amantadine only); dopamine agonists may diminish effects of typical antipsychotics (amantadine only); may diminish effects of influenza virus vaccine
Monitoring	Renal function, Parkinson's symptoms, mental status, influenza symptoms, blood pressure
Case Notes	Adamantanes are the least appropriate choices for treatment of influenza type B in this patient. The adamantanes only have activity against influenza type A, but based on current reports from the Advisory Committee on Immunization Practices (ACIP), 92% of type A influenza viruses are resistant to the adamantanes. Based on this information, neither medication in this class is currently recommended for treatment or prevention of influenza. Adamantanes are currently used as anti-Parkinson's agents and for treatment of extrapyramidal symptoms because of their agonism of dopamine. Amantadine and rimantadine are dosed based on weight and age. Please refer to individual package inserts for full dosing guidelines.

A 15-year-old African-American girl presents to the pediatric clinic for complaints of flu-like symptoms for the past 24 hours. She is complaining of myalgias, headache, nonproductive cough, sore throat, and clear rhinitis. Her mother states she has had a fever for the past 24 hours, with maximum temperature reaching 102.6°F. She is up to date on all vaccinations, but did not receive an influenza vaccine this past fall. She has received the influenza vaccine in the past with no adverse reactions. She lives at home with her mother and father, and she has one brother (age 10 years) who recently was diagnosed with influenza.

Allergies: NKDA

Medications: Acetaminophen 325 mg tablet (OTC) 1 po prn headaches

Physical Exam/Other Studies:

Wt 88 lb Ht 57 in T 102.1°F BP 110/76 HR 86 RR 18 O_2 sat 98%

Physical exam reveals lungs CTA, no crackles on inspiration.

Because of physical exam findings and lack of productive cough, pneumonia is ruled out. Based on history and exposure, influenza is suspected for this woman and treatment should be started today.

What class of medications is most appropriate for treatment of influenza in this patient?

Neuraminidase Inhibitors	Oseltamivir, zanamivir
Mechanism of Action	Provides inhibition of influenza virus neuraminidase, an enzyme known to cleave the budding viral progeny from its cellular envelope attachment point (neuraminic acid) just prior to release
***Contraindications*/ Precautions**	*Hypersensitivity*/Allergic reactions, neuropsychiatric events, respiratory effects, renal impairment, hepatic impairment (oseltamivir only), cardiovascular disease
Adverse Effects	Vomiting, nausea, abdominal pain, diarrhea, conjunctivitis, epistaxis, anemia
Drug Interactions	Live attenuated influenza virus effects may be diminished with concomitant neuraminidase inhibitor therapy. Avoid therapy two days before and two weeks after vaccine administration. Probenecid may increase serum concentrations of oseltamivir active metabolite(s).
Monitoring	Signs or symptoms of unusual behavior, including self-injury, confusion, and/or delirium; critically ill patients should have a repeat test to determine on going viral replication
Case Notes	Neuraminidase inhibitors are the best treatment for influenza. Medication should be initiated within two days of onset of symptoms. Oseltamivir adult dosing is 75 mg po daily for five days. Oseltamivir dosing is weight-based for children aged 12 months to 13 years (refer to drug reference for complete dosing information). Oseltamivir is available in capsule and suspension forms. Zanamivir dosing (adults and pediatrics over the age of 7 years) is available in a powder for inhalation and is dosed two inhalations (10 mg total) po twice daily for five days. Separate zanamivir doses on day one by at least two hours. Doses on subsequent days should be separated by approximately 12 hours. These medications are also used for prevention of influenza. If an individual is in contact with an infected person, prophylaxis should be initiated within two days. Oseltamivir prophylaxis dosing for adults is 75 mg po daily for 10 days. Zanamivir prophylaxis dosing for adults and children >5 is two inhalations (10 mg total) po daily for 10 days.

A 26-year-old woman presents to the pharmacy requesting to speak with you about a personal issue. She tells you she has recently become sexually active and is looking for the easiest method of birth control. Her partner uses protection, but she knows that this method can sometimes fail at preventing pregnancy. She reports that her vaginal skin is very sensitive, so she tries to avoid topical products. She tells you that she exercises regularly, eats a healthy diet, and does not smoke. She occasionally has one to two glasses of beer with dinner and on special occasions. Her only complaints include acne associated with the onset of menses and menstrual cramping. She is a healthy female with no past medical history or diagnoses.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 120 lb Ht 64 in T 98.8°F BP 118/76 HR 80

Physical exam not performed.

What is the best option for birth control for this patient?

Combined Hormonal Contraceptive (CHC)	Estrogen (ethinyl estradiol [EE], mestranol, estradiol valerate)/progestin (norethindrone, norgestrel, ethynodiol diacetate, levonorgestrel, desogestrel, drospirenone, dienogest)
Mechanism of Action	Progestins thicken cervical mucus, preventing sperm penetration, slowing tubal motility, and inducing endometrial atrophy. Estrogens and progestins block the rise in LH, which inhibits ovulation. Estrogens stabilize endometrial lining and provide cycle control.
***Contraindications*/Precautions**	*Hypersensitivity, history/current VTE, thrombophlebitis, history/current stroke or MI, CVD, CAD, valvular heart disease, severe HTN, DM with vascular involvement, severe HA with neurologic symptoms, breast carcinoma, endometrial cancer, estrogen-dependent cancer, prolonged immobilization, heavy smoking and age over 35, pregnancy*/Women over 35 years of age, smoking, hypertension, dyslipidemia, diabetes, migraine headaches, thromboembolism, systemic lupus erythematosus, sickle cell disease
Adverse Effects	Breakthrough bleeding, nausea, and vomiting. Experiencing any red flag adverse effects, known as "ACHES" (abdominal pain, chest pain, headaches, eye problems, severe leg pain), should be reason for immediate discontinuation and physician consultation.
Drug Interactions	Estrogens: substrates of CYP3A4; progestins: substrates of CYP2C19; possibly antibiotics
Monitoring	Pregnancy, ACHES symptoms, BP, depression, glycemic control, lipids, vaginal bleeding
Case Notes	Because this woman does not smoke, is not over age 35, and is experiencing symptoms such as acne and menstrual pain, a combined hormonal contraceptive is a great choice for this patient. CHCs come in more than 30 combinations and strengths. Depending on estrogenic/androgenic symptoms, a patient may need to increase or decrease either the estrogen or progestin component of the CHC. Every woman starting CHC should be counseled on the ACHES warning symptoms as well as proper use of CHCs and potential failure rates. A transdermal patch and vaginal ring are also available as options.

A 60-year-old woman presents to your family medicine clinic complaining of hot flashes. She says she has done a little research on the internet and has talked with her friends and they say there are pills that can help with these hot flashes. She has a history of hypertension, which has been controlled with a prescription for 20 years. She denies alcohol, tobacco, and any other illicit substance use. She does not currently exercise, but says she eats a diet that is "pretty healthy." She does also mention she is experiencing some incontinence episodes. She says they are most likely due to her old age. When asked, she describes that the episodes only occur when she coughs, sneezes, or has to lift heavy boxes. Her past surgical history includes a hysterectomy approximately 15 years ago.

Allergies: NKDA

Medications: Lisinopril/HCTZ 10/25 mg tablet 1 po twice daily; aspirin 81 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 150 lb Ht 65 in T 98.6°F BP 140/82 HR 78 RR 18

She is looking for a medication that can help with her vasomotor menopausal symptoms. Based on her history, you are consulted to assist with the decision.

What class of medications should be prescribed to help treat her current symptoms?

Estrogen	Conjugated equine estrogen, synthetic conjugated estrogen, esterified estrogen, estropipate, micronized estradiol, estradiol acetate
Mechanism of Action	Estrogens modulate secretion of gonadotropins, LH, and FSH; estrogen replacement reduces elevated levels of these hormones in postmenopausal women, decreasing vasomotor symptoms.
***Contraindications*/ Precautions**	*Hypersensitivity, undiagnosed abnormal vaginal bleeding, history/current thromboembolic disorders, active/recent arterial thromboembolic disease, breast cancer, estrogen-dependent tumor, hepatic dysfunction or disease, pregnancy*/Cardiovascular disease, dementia, endometrial carcinoma, lipid effects, ovarian cancer, retinal vascular thrombosis, vaginal bleeding, cholestatic jaundice, endometriosis, diseases associated with fluid retention, GB disease, hypocalcemia, porphyria, SLE
Adverse Effects	Headache, nausea, breast tenderness, heavy bleeding; more serious adverse effects are increased risk for coronary heart disease, stroke, VTE, breast cancer, and gallbladder disease
Drug Interactions	Major substrate of CYP1A2, 3A4; avoid use with anastrozole
Monitoring	BP, pap smear, breast exam, mammogram, signs of endometrial cancer, signs/symptoms of thromboembolic disorders, lipid panel (if diagnosed with dyslipidemia), need for therapy every three to six months, bone density measurement
Case Notes	The goal of estrogen-based hormone replacement therapy is to relieve vasomotor symptoms associated with menopause. Prescribers should be urged to use the lowest effective dose of estrogen for the shortest duration due to the increased risk of breast cancer and arterial and venous thromboembolic risk associated with its use. Estrogen comes in oral, transdermal, intravaginal, intranasal, IM, or SQ dosage forms. Estrogen is also used to treat vulvar and vaginal atrophy, hypoestrogenism, prostatic cancer, breast cancer, abnormal uterine bleeding, dyspareunia, and stress incontinence. A benefit of estrogen is reduction in osteoporosis risk.

A 45-year-old woman presents to your clinic complaining of a recent onset of vasomotor symptoms. She is having episodes approximately 15 times a day and finds them unbearable. She has a past medical history of asthma and allergic rhinitis. She has not had a hysterectomy.

Allergies: NKDA

Medications: Fluticasone/salmeterol 250/50 mcg inhalation 1 puff po twice daily; fexofenadine 60 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 180 lb Ht 68 in T 97.6°F BP 122/84 HR 80 RR 18

Physical exam reveals no pertinent findings.

Spirometry exam deferred.

After risks and benefits are reviewed with the patient, she decides she would like to try oral therapy to treat her vasomotor symptoms. Because of her past medical history, she should be prescribed low-dose estrogen in combination with another drug class.

What class of medications should be added to her estrogen therapy for her vasomotor symptoms?

Progestin	Dydrogesterone, medroxyprogesterone acetate, micronized progesterone, norethisterone, norethindrone acetate, norgestrel, levonorgestrel, etonogestrel
Mechanism of Action	Inhibits secretion of pituitary gonadotropins, which prevent follicular maturation and ovulation; causes endometrial thinning
Contraindications/ Precautions	*Hypersensitivity, history/current thromboembolic disorders, cerebrovascular disease, severe hepatic dysfunction or disease, carcinoma of the breast or genital organs, undiagnosed vaginal bleeding, missed abortion, pregnancy*/Bone mineral density loss, long-term use, breast cancer, dementia, retinal vascular thrombosis, cardiovascular disease, depression, diabetes, diseases exacerbated by fluid retention, osteoporosis
Adverse Effects	Irritability, depression, headache, mood swings, bloating, fluid retention, sleep disturbance, weight changes, decreased libido, dizziness, nervousness, abdominal pain, weakness, edema, acne, alopecia, breast pain
Drug Interactions	Major substrate of CYP3A4
Monitoring	Breast/pelvic exam including pap smear prior to initiation of therapy, rule out pregnancy, monitor for signs/ symptoms of thromboembolic disorders, depression, glucose, blood pressure
Case Notes	Progestins are added to estrogen therapy for postmenopausal women who have not had a hysterectomy due to the increased risk of endometrial hyperplasia with estrogen therapy alone. When dosed with cyclic estrogen therapy for postmenopausal women, progestins should be taken for 12-14 days of the month, starting either on day 1 or day 16 of the cycle. Lower doses can be used if given concomitantly with estrogen throughout the entire cycle. Prescribers should be urged to use the lowest effective dose of estrogen for the shortest duration due to the potential risks of its use. Combined products do exist for patients in need of estrogen/progestin therapy. Progestins can be used for birth control if other methods are inadequate.

A 28-year-old woman presents to your pharmacy to pick up prescriptions. When she gets to the register, she tells you that you may return her oral contraceptive pills to the shelf because she will not need them. She then shares with you that she just found out she is pregnant and wants to know if there is anything specific she should add to her daily diet before she goes to see her OB/GYN in about a month.

Allergies: NKDA

Medications: Ethinyl estradiol/levonorgestrel 20 mcg/0.1 mg tablet 1 po daily (self-discontinued approximately three weeks ago)

Physical Exam/Other Studies:

Wt 110 lb Ht 62 in

What vitamin should you recommend she take during her pregnancy?

Folic Acid	Water-soluble vitamin (ascorbic acid, cyanocobalamin, folic acid, hydroxocobalamin, niacin, pantothenic acid, pyridoxine, riboflavin, thiamine)
Mechanism of Action	Folic acid is necessary for formation of a number of coenzymes in many metabolic systems, particularly for purine and pyrimidine synthesis; required for nucleoprotein synthesis and maintenance in erythropoiesis; stimulates WBC and platelet production in folate deficiency anemia
Contraindications/ **Precautions**	*Hypersensitivity/*Anemia, pernicious anemia, benzyl alcohol (found in injection)
Adverse Effects	Bronchospasm, erythema, flushing, malaise, pruritus, rash
Drug Interactions	Avoid use with raltitrexed; levels of phenobarbital, phenytoin, primidone, raltitrexed may be reduced
Monitoring	Monitor for adverse effects
Case Notes	Recommended daily allowance for folic acid is 0.4 mg daily. Folic acid requirements increase during pregnancy. To prevent tubal defects such as anencephaly and spina bifida, a pregnant female should take 0.4-0.8 mg/day. A female with anemia during pregnancy or lactation should take 0.8 mg/day. A female with family history of neural tube defects should take 4 mg/day. Folic acid is also used to treat megaloblastic and macrocytic anemias due to folate deficiency. Vitamin B_{12} deficiency should be ruled out before starting folic acid for anemia. Foods such as dried beans, nuts, bran, vegetables, and fruits also contain folic acid. Excessive use of alcohol increases requirement for folic acid. Folic acid is available as a tablet (0.4 mg, 0.8 mg, 1 mg) or injection (5 mg/mL, 10 mL).

A 78-year-old woman presents to your pharmacy and asks to speak to you in private. She tells you that she is horribly embarrassed because she can no longer do the things she enjoys doing because of a problem she is having. She tells you that she sometimes has episodes of incontinence, and it keeps her from being active or going out in public. She says she finds herself running to the bathroom on occasion, with some episodes occurring with very little warning. She hopes that there is something you can recommend for her to take that will solve her problem. She also suffers from hypertension and dyslipidemia.

Allergies: Sulfa (anaphylaxis)

Medications: Lisinopril 20 mg tablet 1 po twice daily; nicotinic acid sustained release 500 mg tablet 1 po twice daily; aspirin 81 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 140 lb Ht 66 in BP 128/80 HR 80

Physical exam not performed.

You mention to the patient that there are medications that may help her symptoms. You tell her that she will need to be seen at her doctor's office to properly be managed, but that you can discuss the medication she will most likely need today.

What medication class is the best choice in this patient to treat her urinary incontinence?

Antispasmodic/ Anticholinergic	Oxybutynin, fesoterodine, tolterodine, trospium chloride, solifenacin, darifenacin
Mechanism of Action	Direct antispasmodic effect on smooth muscle, also inhibits the action of acetylcholine on smooth muscle; increases bladder capacity, decreases uninhibited contractions, and delays desire to void, therefore, decreases urgency and frequency
***Contraindications*/ Precautions**	*Hypersensitivity, uncontrolled narrow-angle glaucoma, urinary retention, gastric retention, or conditions with severely decreased GI motility*/Anticholinergic effects, CNS depression, heat prostration, autonomic neuropathy, cardiovascular disease, dementia, GI disorders, glaucoma, hepatic or renal impairment, hiatal hernia, hyperthyroidism, myasthenia gravis, prostatic hyperplasia/urinary stricture, elderly patients
Adverse Effects	Dizziness, somnolence, xerostomia, constipation, nausea, headache, pain, nervousness, diarrhea, dyspepsia, urinary hesitation/retention, blurred vision, dry eyes, rhinitis, weakness
Drug Interactions	May increase levels of anticholinergics, cannabinoids, potassium chloride; levels of oxybutynin may be increased by pramlintide; may decrease levels of acetylcholinesterase inhibitors; caution with use of ethanol
Monitoring	Incontinence episodes, postvoid residual
Case Notes	An anticholinergic/antispasmodic agent is first-line treatment in overactive bladder. Geriatric patients should be observed closely while on this medication because of the anticholinergic activity and subsequent increased risk for side effects. Dose adjustments should be made for patients with renal or hepatic impairment. Gel, syrup, and patch formulations are also options for patients. Drug holidays may help to determine if the need for medication still exists. Long-acting formulations as well as newer agents (eg, darifenacin, solifenacin, trospium, fesoterodine) carry a lower risk of anticholinergic side effects. Weigh risks versus. benefits for each patient in picking the most appropriate agent.

A 69-year-old man presents to his primary care provider with a complaint of decreased sexual function. He has noticed a loss of interest in sexual activity as well as a decreased ability to achieve and maintain an erection. His medical history is significant for hypertension and dyslipidemia.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; simvastatin 80 mg tablet 1 po at bedtime; metoprolol 50 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 199 lb Ht 71 in T 98.6°F BP 142/78 sitting HR 76 RR 20 TC 198 LDL 122
HDL 45 TG 155 SCr 1.0 Free testosterone 5 LH 2 Serum prolactin 18
All other labs were within normal limits.
His physician diagnoses him with erectile dysfunction (ED) and hypogonadism.

In addition to a PDE-5 inhibitor, which medication may benefit the patient?

Testosterone	Androgens (testosterone, methyltestosterone)
Mechanism of Action	Supplementation of endogenous testosterone
***Contraindications*/ Precautions**	*Hypersensitivity, breast or prostate carcinoma, serious renal, hepatic, or cardiac disease, pregnancy or breast feeding*/Gynecomastia, hypercalcemia, hepatic dysfunction, hypoglycemia, prostate cancer, benign prostatic hypertrophy, edema, sleep apnea, secondary exposure to pediatric patients with gel formulation
Adverse Effects	Acne, edema, gynecomastia, deep venous thrombosis, aggressive behavior, alopecia
Drug Interactions	Testosterone may increase levels of cyclosporine or vitamin K antagonists
Monitoring	Testosterone level, liver function tests, PSA and prostate exams, lipid profile, CBC, glucose (in patients with diabetes)
Case Notes	Testosterone replacement may increase libido and improve sexual dysfunction in patients with hypogonadism and very low free testosterone levels (<7-8 pg/mL) as in this patient. Testosterone is available in several formulations. Topical and injectable formulations are preferable to oral formulations at normalizing serum testosterone levels due to increased bioavailability and reduced adverse effects. Long-acting intramuscular testosterone is the treatment of choice for primary hypogonadism at a dose of 50-400 mg administered every two to four weeks. Topical formulations may also be effective at doses of 2.5-7.5 mg/day (transdermal patch), 5 g/day (gel), and 30 mg every 12 hours (buccal). Testosterone is a pregnancy category X, so females of child-bearing age should avoid contact with skin where topical formulations have been applied. Additionally, transfer of the gel may occur by skin-to-skin contact, which could expose nonusers to the effects of the gel. This secondary exposure to children and females has resulted in virilization. Care should be taken to avoid exposure of application sites to other individuals.

A 70-year-old man presents to his primary care provider. He has noticed that he is having difficulty urinating regularly. He urinates several times daily and at night will wake up two to three times with the need to urinate. Regardless of how often he urinates, he still feels the urge to go. He has a history of allergic rhinitis and asthma for 55 years. Last year, he suffered from a hip fracture and required surgical repair. He is still using a walker to ambulate, so he is very concerned about making it to the bathroom "in time."

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; albuterol MDI 1-2 puffs every four to six hours as needed for symptoms; fluticasone MDI 220 mcg 2 puffs in the morning and evening; diphenhydramine 25 mg capsule (OTC) 1 po daily at bedtime; tramadol 50 mg tablet 1 po every four hours as needed for hip pain

Physical Exam/Other Studies:

Wt 176 lb Ht 71 in T 98.6°F BP 112/78 sitting HR 78 RR 20 SCr 1.1 PSA 4.0

Urinalysis reveals no signs of urinary tract infection.

On physical exam, the prostate is enlarged (45 g) and benign.

He is given a diagnosis of benign prostatic hypertrophy (BPH). His symptoms are moderate, so his physician would like to start a medication to improve symptoms and quality of life.

Which medication class would be the best option for this patient?

5-Alpha Reductase Inhibitors	Finasteride, dutasteride
Mechanism of Action	Inhibition of type II 5-alpha reductase, which reduces the enlargement of the prostate gland by testosterone stimulation
***Contraindications/* Precautions**	*Hypersensitivity*/Teratogenic—women desiring pregnancy or who are pregnant should avoid handling the tablets, hepatic impairment, obstructive uropathy, prostate cancer
Adverse Effects	Sexual dysfunction, nausea, abdominal pain, dizziness, flatulence, headache, rash, muscle weakness, gynecomastia
Drug Interactions	No known drug interactions exist.
Monitoring	PSA, prostate exams, symptom control
Case Notes	Both 5-alpha reductase inhibitors and alpha$_1$-adrenergic blockers are equally effective in controlling the symptoms of BPH. However, alpha$_1$-adrenergic blockers may cause pronounced orthostatic hypotension and may increase the risk of falls, so in this patient with mobility difficulties, these may not be the best option. To see clinical benefit, 5-alpha reductase inhibitors may need to be taken for up to 6-12 months. They can be used in combination with alpha$_1$-adrenergic blockers in patients who require fast symptom relief or in patients who do not respond fully to treatment. 5-alpha reductase inhibitors are effective in reducing the size of the prostate and are indicated in men with enlarged prostates of at least 40 g with BPH. They do cause more sexual dysfunction than alpha$_1$-adrenergic blockers. Doses typically used in the treatment of BPH are: finasteride (5 mg daily); dutasteride (0.5 mg daily). It is also important in men with BPH to assess the medication profile for medications that may exacerbate their condition and symptoms. Medications that may worsen BPH include anticholinergics or adrenergic agents. In this patient, changing his diphenhydramine to an intranasal corticosteroid may also improve his BPH symptoms while controlling his allergic rhinitis.

A 70-year-old man presents to his primary care provider. He has noticed that he is having difficulty urinating regularly. He urinates several times daily and at night will wake up two to three times with the need to urinate. Regardless of how often he urinates, he still feels the urge to go. He has a history of allergic rhinitis and asthma × 55 years, and hip fracture/surgical repair × 1 year. Six months ago, his physician began finasteride to treat benign prostatic hypertrophy (BPH) symptoms. However, he is still having increased urge to urinate and weak urinary flow.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; albuterol MDI 1-2 puffs every four to six hours as needed for symptoms; fluticasone MDI 220 mcg 2 puffs in the morning and evening; beclomethasone nasal spray 42 mcg 1 spray in each nostril daily; calcium carbonate 600 mg + 400 IU vitamin D tablets (OTC) 1 po twice daily; finasteride 5 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 176 lb Ht 71 in T 98.6°F BP 112/78 sitting HR 78 RR 20 SCr 1.1 PSA 5.0

Urinalysis reveals no signs of urinary tract infection.

On physical exam, the prostate is enlarged (40 g) and benign. His prostate size has reduced since beginning the finasteride.

Which medication class could be added to improve his BPH symptoms?

Alpha$_1$-Blockers	Prazosin, alfuzosin, terazosin, doxazosin, tamsulosin
Mechanism of Action	Blockade of alpha$_1$-adrenergic receptors in prostatic tissue resulting in smooth muscle relaxation
***Contraindications*/ Precautions**	*Hypersensitivity, hepatic impairment (alfuzosin), concurrent use with CYP3A4 inhibitors (alfuzosin)*/ Hypotension, vision disorders, angina, sulfonamide allergy (tamsulosin), hepatic or renal impairment (alfuzosin), QT prolongation (alfuzosin)
Adverse Effects	First-dose syncope, orthostatic hypotension, dizziness, ejaculatory dysfunction
Drug Interactions	Levels may be decreased by CYP3A4 inhibitors, calcium channel blockers; other medications capable of causing hypotension or vasodilatation may increase adverse effects
Monitoring	Blood pressure (standing and supine), symptom control
Case Notes	Both 5-alpha reductase inhibitors and alpha$_1$-adrenergic blockers are equally effective in controlling the symptoms of BPH and are both considered first-line agents for treatment of BPH. To see clinical benefit, 5-alpha reductase inhibitors may need to taken for up to 6-12 months. Therefore, alpha$_1$-adrenergic blockers may be preferred in patients who required fast symptom relief or in patients who do not respond fully to treatment with 5-alpha reductase inhibitors alone. Alpha$_1$-blockers do cause pronounced hypotension, so they would not be an appropriate choice in patients who cannot tolerate reduced blood pressures such as those with severe arrhythmias or severe cardiac disease. Also, they may not be a good initial choice for patients at risk for falling. Patients should be educated on the adverse effects of these drugs and specifically warned about first-dose syncope. Tamsulosin is a selective alpha$_{1A}$-blocker with low affinity for vascular smooth muscle, so it has a lower risk of causing hypotension. Doses typically used in the treatment of BPH are: prazosin (2-10 mg/day in two to three divided doses, not recommended due to multiple daily dosing); terazosin (1-10 mg/day); doxazosin (4 or 8 mg/day immediate release, 10 mg/day XL); alfuzosin (10 mg/day); tamsulosin (0.4 or 0.8 mg/day).

A 45-year-old man with diabetes presents to his primary care provider with a complaint of decreased sexual function. He has had an inability to develop and maintain an erection for the last two to three months. He has a history of diabetes and dyslipidemia. He smokes half of a pack of cigarettes per day and only occasionally drinks a beer or glass of wine with dinner.

Allergies: NKDA

Medications: Aspirin 81 mg chewable tablet (OTC) 1 po daily; simvastatin 40 mg tablet 1 po at bedtime; enalapril 10 mg tablet 1 po twice daily; 70/30 insulin 45 units subcutaneously with breakfast and 50 units subcutaneously with the evening meal

Physical Exam/Other Studies:

Wt 192 lb Ht 70 in T 98.6°F BP 122/78 sitting HR 78 RR 18 A1c 8.2% TC 188
LDL 112 HDL 45 TG 155 SCr 1.1 Free testosterone 80 LH 4 Serum prolactin 18
All other labs were within normal limits.
His physician diagnoses him with erectile dysfunction (ED).

Since the patient's lab tests do not suggest hypogonadism at this point, which class of medications would be an appropriate first-line option?

Phosphodiesterase-5 Enzyme Inhibitors (PDE-5 inhibitors)	Sildenafil, tadalafil, vardenafil
Mechanism of Action	Selective inhibition of cGMP-specific phosphodiesterase-5 enzyme, resulting in enhanced nitric oxide-induced smooth muscle relaxation of the corpus cavernosum during sexual stimulation
***Contraindications*/ Precautions**	*Hypersensitivity, concurrent use of any form of nitrates*/Hypotension, priapism, pulmonary edema, deformation of the penis, bleeding disorders, uncontrolled or serious cardiovascular disease, pulmonary artery hypertension, peptic ulcer disease, hepatic or renal impairment, vision or hearing disorders
Adverse Effects	Headache, dyspepsia, flushing, insomnia, diarrhea, abnormal vision changes (blue/green color discrimination decreased), epistaxis, increased liver function tests
Drug Interactions	Nitrates, antihypertensives, vasodilators. PDE-5 inhibitor levels may be increased by CYP3A4 inhibitors and decreased by CPY3A4 inducers.
Monitoring	Assess for potential drug interactions with prescription and nonprescription medications
Case Notes	PDE-5 inhibitors would be an appropriate choice in this patient since there is nothing at this point to suggest hypogonadism. Hypogonadism might necessitate the use of hormonal agents, such as testosterone, to treat the erectile dysfunction. Control of diseases that contribute to the development of ED (eg, diabetes, dyslipidemia, tobacco dependence) is important as well. The use of nitrates and PDE-5 inhibitors should always be avoided. The combination has increased the risk of hypotension, myocardial infarction, and death. Patients with active coronary ischemia, heart failure, low blood pressure, or using multiple antihypertensives may be at risk for serious cardiac adverse effects if using PDE-5 inhibitors. Dosing: sildenafil (50 mg po × 1 dose, 100 mg/day max); tadalafil (10 mg po × 1 dose, 20 mg/day max); vardenafil (10 mg po × 1 dose, 20 mg/day max). Doses should be taken approximately one hour prior to intercourse. Effects from sildenafil and vardenafil last approximately four hours; tadalafil's effects may last up to 36 hours.

A 58-year-old woman comes to the geriatric clinic with her daughter. She has become increasingly forgetful lately of names and dates, even forgetting how to turn off the car before she gets out of it when driving. Her daughter brought her to the clinic today. Her only current medical condition is glaucoma.

Allergies: NKDA

Medications: Latanoprost ophthalmic solution 0.005% 1 drop in each eye once daily in the evening

Physical Exam/Other Studies:

Wt 130 lb Ht 65 in T 98.6°F BP 132/84 sitting 128/80 standing HR 76 RR 18

Urinalysis, ECG, and chest x-ray were normal. All other labs and tests were within normal limits. Physical exam reveals a well-groomed female who gets irritated when asked about her symptoms. A Folstein mini-mental status exam was administered, and her score was 22/30. Her Blessed Dementia Scale score is 25/33.

A diagnosis of Alzheimer's disease is made. She is staged as having mild cognitive decline.

What class of medications would be appropriate to begin in this patient?

Cholinesterase Inhibitors	Donepezil, rivastigmine, galantamine
Mechanism of Action	Reversibly inhibit acetylcholinesterase activity in the CNS. Galantamine also stimulates nicotinic receptors, and rivastigmine inhibits both acetylcholinesterase and butyrylcholinesterase activity in the CNS.
***Contraindications*/ Precautions**	*Hypersensitivity, severe liver dysfunction (galantamine)*/Anorexia or weight loss, gastrointestinal effects, vagotonic effects, cardiac conduction abnormalities, peptic ulcer disease, respiratory disease, seizure disorder, urinary tract obstruction
Adverse Effects	Nausea, anorexia, vomiting, diarrhea, headache, bradycardia
Drug Interactions	Succinylcholine, antipsychotics, beta-blockers, cholinergic agonists, anticholinergics, neuromuscular-blocking agents, corticosteroids, SSRIs
Monitoring	Behavior, mood, cognitive function and ability to perform activities of daily living, bowel function
Case Notes	Cholinesterase inhibitors are indicated for the treatment of mild to severe Alzheimer's disease. They are the first-line agents in the treatment of this disease. However, no cholinesterase inhibitor has been proven to prevent progression of Alzheimer's disease or produce a long-lasting improvement in symptoms. One additional cholinesterase inhibitor, tacrine, is currently available. However, hepatotoxicity associated with this agent has resulted in a discontinuation of use of the product. No cholinesterase inhibitor is preferred over another. Donepezil and galantamine can be given as a single daily dose. Rivastigmine is available as a transdermal patch as well as an oral formulation. Donepezil (CYP3A4) and galantamine (CYP3A4, CYP2D6) are metabolized by cytochrome P450 isoenzymes. The goals of treatment with these agents are to slow cognitive decline with the agent that produces the best effect with the least amount of adverse effects. GI adverse effects tend to be the dose-limiting effects in patients.

A 62-year-old woman comes to the geriatric clinic with her daughter. She has been taking donepezil for about two years. However, now her family is noticing some new cognitive decline. Her medical conditions include Alzheimer's disease, glaucoma, and osteopenia.

Allergies: NKDA

Medications: Donepezil 10 mg tablet 1 po daily; latanoprost ophthalmic drops 0.005% 1 drop in each eye once daily in the evening; calcium carbonate 600 mg/vitamin D 400 IU tablet (OTC) 1 po twice daily

Physical Exam/Other Studies:

Wt 124 lb Ht 65 in T 98.6°F BP 124/84 sitting 120/80 standing HR 72 RR 18

A Folstein mini-mental status exam was administered, and her score was 23/30 when she was diagnosed. Her score today is 18/30.

Her physician considers her disease to be more advanced and in the moderate stage.

What medication could be added for her worsening Alzheimer's disease?

Memantine	N-methyl-D-aspartate (NDMA) receptor antagonist (no other agents)
Mechanism of Action	Uncompetitive antagonist of the NDMA glutamate receptors in the brain
***Contraindications*/ Precautions**	*Hypersensitivity*/Hepatic impairment, renal impairment, seizure disorder
Adverse Effects	Headaches, dizziness, hallucinations, hypertension
Drug Interactions	Trimethoprim, carbonic anhydrase inhibitors, sodium bicarbonate
Monitoring	Behavior, mood, cognitive function, and ability to perform activities of daily living
Case Notes	Glutamate is an excitatory amino acid in the CNS. Overstimulation of glutamate receptors may lead to cell death. Memantine, by antagonizing the NDMA type of glutamate receptors, may improve cognitive function in Alzheimer's disease. It is indicated for moderate-to-severe disease, and may be added with acetylcholinesterase inhibitors in patients who are no longer responding to monotherapy. Overall, memantine provides modest benefit in Alzheimer's disease. There are several agents that are currently being researched for benefit in prevention of Alzheimer's. These include NSAIDs, MAO-B inhibitors and gingko biloba. However, at this time, none of these agents has shown a significant benefit.

A 25-year-old woman presented to the emergency department after having a seizure. She had an episode beginning with an unusual sensation of smelling a strong odor and a feeling of unease which was followed by an involuntary twitching of her arms that she could not control. She remained conscious throughout the episode. She remembers that, as a younger child, she had some febrile seizures and was treated briefly, but she cannot remember the name of the drug. She has had other episodes like this in the last few months, but they were not as severe as this episode. Her medical history is significant for a pulmonary embolism, which occurred six weeks ago. She was diagnosed with a thrombophilia and is now on long-term anticoagulation therapy.

Allergies: NKDA

Medications: Combined oral contraceptive tablet 1 po daily; warfarin 2 mg tablet 1 po Monday, Wednesday, and Friday and 1/2 tablet on Tuesday, Thursday, Saturday, and Sunday

Physical Exam/Other Studies:

Wt 110 lb Ht 64 in T 98.6°F BP 110/70 HR 80 RR 18

All labs are WNL.

EEG shows changes consistent with partial seizure disorder.

A diagnosis of seizure disorder is made, and her physician is planning to begin antiepileptic drug therapy.

Which antiepileptic may interact with her warfarin therapy?

A. carbamazepine
B. gabapentin
C. levetiracetam
D. lamotrigine

Carbamazepine	Antiepileptic drug (AED): enzyme inducers (carbamazepine, phenytoin, phenobarbital, primidone, oxcarbazepine); enzyme inhibitors (valproic acid)
Mechanism of Action	Carbamazepine, phenytoin, and oxcarbazepine block sodium channels. Phenobarbital, primidone, and valproic acid increase GABA activity.
***Contraindications*/ Precautions**	*Hypersensitivity to individual agents*/Pregnancy, CNS depression, dermatologic reactions, renal or hepatic dysfunction, blood dyscrasias. Multiple contraindications/precautions exist—consult product information for a complete list for each individual agent.
Adverse Effects	Somnolence, dizziness, drowsiness, ataxia, skin rash, blood dyscrasias (carbamazepine)
Drug Interactions	Multiple interactions exist—consult product information for individual agents. Carbamazepine induces CYP3A4, 1A2, and 2C and glucuronyltransferase; phenytoin and phenobarbital induce CYP1A2 and 2C and glucuronyltransferase; primidone induces CYP1A2, 2B6, 2C9, and 3A4; oxcarbazepine induces CYP3A4; valproic acid inhibits CYP2C19 and may induce CYP3A (dose dependent).
Monitoring	Seizure episodes, renal and hepatic function, serum blood levels of AED, CBC
Case Notes	The choice of AED for seizure varies based on patient-specific factors and type of seizure. Multiple options exist for each type of seizure. In this patient case, because of the potential drug interaction with carbamazepine, any of the other antiepileptic choices would be preferable. Carbamazepine, phenytoin, phenobarbital, primidone, and oxcarbazepine are strong inducers of CYP isoenzymes that can result in decreased blood levels of CYP isoenzymes substrates, including warfarin. Valproic acid is a CYP enzyme inhibitor, which may increase blood levels of CYP substrates. Many AEDs are potentially teratogenic, so it is important to counsel patients about this risk. Additionally, many AEDs can decrease contraceptive efficacy, so it is especially important to consider this drug interaction in women of childbearing age when selecting an AED.

An 18-year-old man is diagnosed with generalized seizure disorder. His past medical history is significant for asthma.

Allergies: NKDA

Medications: Theophylline 200 mg XR tablet 1 po every eight hours; albuterol MDI 2-4 puffs as needed for asthma symptoms

Physical Exam/Other Studies:

Wt 160 lb Ht 71 in T 98.6°F BP 112/78 HR 81 RR 18

All labs are WNL.

Serum theophylline concentration 12 mcg/mL.

Which antiepileptic drug would not decrease his theophylline serum concentration?

A. carbamazepine
B. phenytoin
C. phenobarbital
D. topiramate

Topiramate	Antiepileptic drug (AED) Non-inducer/inhibitors (ethosuximide, felbamate, gabapentin, lacosamide, lamotrigine, levetiracetam, pregabalin, tiagabine, topiramate, zonisamide)
Mechanism of Action	Reduction of seizures through multiple mechanisms. Topiramate, lacosamide, lamotrigine, and zonisamide block sodium channels. Tiagabine and gabapentin have activity at GABA receptors or inhibit the degradation of GABA. Ethosuximide inhibits T-type calcium channels. Felbamate blocks glycine on NMDA receptors. The exact mechanism of action is unknown for gabapentin, pregabalin, and levetiracetam.
***Contraindications*/ Precautions**	*Hypersensitivity to individual agents*/Pregnancy, CNS depression, renal or hepatic dysfunction. Multiple contraindications/precautions exist—consult product information for a complete list for each individual agent.
Adverse Effects	Somnolence, dizziness, drowsiness, ataxia
Drug Interactions	None of the agents listed significantly induces or inhibits CYP450 metabolism. The drug levels of ethosuximide, felbamate, lamotrigine, tiagabine, topiramate, and zonisamide may be decreased by enzyme inducers (eg, phenytoin, phenobarbital, carbamazepine).
Monitoring	Seizure episodes, renal and hepatic function, CBC, ECG (lacosamide)
Case Notes	The newer antiepileptic drugs, such as topiramate, are not associated with CYP enzyme induction as are older agents, such as carbamazepine, phenytoin, primidone, and phenobarbital. They would be preferable in patients who may be on a medication like theophylline in which a drug interaction may exist. Although most of these agents do not require therapeutic blood level monitoring, they are not without toxicities. Some examples of specific toxicities include: hepatotoxicity or aplastic anemia with felbamate (only used for refractory seizures); heart block with lacosamide; and kidney stones with topiramate and zonisamide.

A 34-year-old woman presents to your pharmacy complaining of headaches. She was recently started on daily topiramate for headache control but says she is still having approximately two headaches a week that keep her home from work. Each headache lasts approximately 24 hours, and she experiences nausea, photophobia, and phonophobia during the headache. Before the headache begins, she can sense she "just doesn't feel right" but doesn't take any medications. To control her headaches, she usually takes ibuprofen 200 mg tablets 2 po every four to six hours without much relief. Her past medical history is positive for migraines, but she is otherwise healthy.

Allergies: NKDA

Medications: Topiramate 25 mg tablet 1 po every evening; ibuprofen 200 mg tablet (OTC) 2 po every four to six hours as needed

Physical Exam/Other Studies:

Wt 125 lb Ht 65 in

Physical exam not performed.

This patient is not getting adequate relief from her current migraine therapy. She asks what medication you recommend to help treat her migraine headaches so she can discuss it with her doctor.

What medication is most appropriate to treat this patient's migraine headache?

A. naproxen
B. sumatriptan
C. butalbital/acetaminophen/caffeine
D. ergotamine tartrate

Sumatriptan	Selective 5-$HT_{1B,1D}$ receptor agonist (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, zolmitriptan)
Mechanism of Action	Selective agonist for serotonin in cranial arteries; causes vasoconstriction and reduces neurogenic inflammation associated with migraine headaches
Contraindications/ Precautions	*Hypersensitivity, ischemic heart disease; cerebrovascular disease, peripheral vascular disease, uncontrolled hypertension, use within 24 hours of ergotamine derivatives, another 5-HT_1 agonist, use within two weeks of discontinuing an MAO inhibitor, management of hemiplegic or basilar migraine, severe hepatic impairment*/Cardiac events, cerebrovascular events, elevated blood pressure, coronary artery disease, hepatic impairment, seizure disorders, MAO inhibitors, serotonin syndrome
Adverse Effects	Dizziness, vasoactive sensations, paresthesia, chest discomfort, hyper/hypotension, burning sensation, flushing, headache, nausea, vomiting, numbness, weakness, diaphoresis
Drug Interactions	Avoid use with ergot derivatives, MAO inhibitors, sibutramine
Monitoring	Resolution of migraine symptoms, cardiovascular response, adverse effects
Case Notes	Sumatriptan is the best medication to abort this patient's migraines. NSAIDs are effective for mild to moderate migraine headaches, but since ibuprofen is not working in this patient, naproxen is not a good choice. Butalbital/acetaminophen/caffeine combination is not appropriate in this patient. There are no data to support or refute the use of this medication in migraines, plus it has addictive properties. Ergotamine is an option, but because of the nonselective agonism of the 5-HT_1 receptor, the side effects will be greater than with sumatriptan. Multiple dosage forms are available for medications in this class, including subcutaneous injectable products, oral disintegrating tablets, and nasal sprays. A combination product exists of sumatriptan and naproxen. Topiramate in this patient should also be increased to help with migraine prophylaxis.

A 42-year-old woman was recently diagnosed with relapsing-remitting multiple sclerosis (MS). Her medical history is significant for severe depression.

Allergies: NKDA

Medications: Fluoxetine 20 mg capsule 1 po every morning; trazodone 150 mg XR tablet 1 po at bedtime

Physical Exam/Other Studies:

Wt 162 lb Ht 68 in T 98.6°F BP 110/70 HR 77 RR 18

All labs are WNL.

Which of the following is the best agent with which to begin treatment of her multiple sclerosis?

A. natalizumab
B. glatiramer acetate
C. interferon beta-1a
D. interferon beta-1b

Glatiramer Acetate	Biologic agent for treatment of MS
Mechanism of Action	Exact mechanism is unknown. It is thought to involve induction, activation, and alteration of T cells.
***Contraindications*/ Precautions**	*Hypersensitivity*/History of systemic reactions postinjection, renal impairment, not for IV administration, neutralizing antibodies may form to glatiramer acetate, elderly or pediatric patients
Adverse Effects	Flushing, chest pain, injection pain, anxiety, shortness of breath, injection site reactions, weakness, infection, diaphoresis, flu-like syndrome, back pain, pruritus, nausea, lipoatrophy, immune response reactions
Drug Interactions	BCG, natalizumab, pimecrolimus, topical tacrolimus, live virus vaccines, leflunomide
Monitoring	Symptoms of MS, efficacy
Case Notes	Glatiramer acetate would be an appropriate treatment option for relapsing-remitting MS. Other first-line options include beta interferons 1a and 1b. However, in patients with pre-existing depression, these agents are used with caution and are contraindicated in patients with severe depression (such as this patient) because beta interferons may worsen depression symptoms. Glatiramer is a first-line agent appropriate for patients with depression who should not use beta interferons. Both beta interferons and glatiramer acetate decrease disease relapse by approximately 30%. Natalizumab is a monoclonal antibody treatment for MS. However it has been associated with a risk of progressive multifocal leukoencephalopathy so it is generally reserved for second-line treatment. Injection site reactions such as redness, swelling, and pain are the most common adverse effects associated with beta interferons and glatiramer acetate. Using ice packs on the injection sites pre- and post-injection and rotating the injection sites will help decrease the severity of these reactions.

A 68-year-old woman with Parkinson's disease presents to her primary care provider with complaints of worsening symptoms. She was diagnosed with the disease eight years ago and has been taking pramipexole and carbidopa/levodopa for the last five years. She has noticed that her carbidopa/levodopa is wearing off and not lasting until the next dose. Her tremor is worse when the dose wears off and she has more difficulty moving because she feels stiff. Her medical history is also significant for depression.

Allergies: Sulfonamides (rash)

Medications: Carbidopa/levodopa 25/100 CR tablet 1 po three times daily; ropinirole 8 mg XL tablet 1 po daily; citalopram 20 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 132 lb Ht 65 in T 98.6°F BP 115/68 sitting 108/60 standing HR 72 RR 18

All other labs were within normal limits.

What medication class could be added to help reduce the motor complications that she is having?

Catechol-*O*-Methyl Transferase Inhibitor (COMT inhibitor)	Entacapone, tolcapone
Mechanism of Action	Inhibits the peripheral breakdown of levodopamine by catechol-*O*-methyl transferase, which increases the amount that crosses the blood-brain barrier to be converted to dopamine in the brain
***Contraindications*/ Precautions**	*Hypersensitivity, history of liver disease (tolcapone), rhabdomyolysis or hyperpyrexia (tolcapone)*/Liver injury, diarrhea, hallucinations, mood disorders, melanoma, neuroleptic malignant syndrome, orthostatic hypotension, rhabdomyolysis, pleural/retroperitoneal fibrosis, dyskinesias, renal or hepatic impairment, cardiovascular disease
Adverse Effects	Dyskinesias, nausea, diarrhea, urine discoloration, hallucinations, vivid dreams, orthostatic hypotension, somnolence or sleep disorders
Drug Interactions	CNS depressants, MAO inhibitors, COMT substrates
Monitoring	Efficacy, dyskinesias, mental status changes, blood pressure, liver function tests, serum iron if anemic
Case Notes	After five years on levodopa therapy, 50-90% of patients taking levodopa will develop some type of movement disorder. These movement disorders can be reduced by adding an COMT inhibitor or dopamine agonist to the regimen. Alternative strategies include adding a MOA-B inhibitor. However, in this patient, that would not be a good choice since she is on an SSRI that would interact with MAO-B inhibitors. Amantadine or anticholinergic agents could also be added to the patient's regimen, but they are less effective than other therapies. Finally, early in therapy, adjusting the dose or the timing of the dose can also be effective in improving dyskinesias. Of the two COMT inhibitors, entacapone is the preferred agent and is also available in a single tablet combination with carbidopa/levodopa. Tolcapone has been associated with liver failure so it is reserved for patients unable to take other therapies.

A 55-year-old man has been diagnosed with Parkinson's disease. His symptoms include mild-to-moderate resting tremor in his right hand, cogwheel rigidity in his extremities, bradykinesia, and a blank facial expression. His balance and coordination are steady. His gait is slow. His medical history includes benign prostatic hypertrophy and osteoarthritis. His symptoms have started to affect his ability to perform his activities of daily living.

Allergies: NKDA

Medications: Acetaminophen 1,000 mg tablet (OTC) 1 po twice daily; multivitamin tablet (OTC) 1 po daily; finasteride 5 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 192 lb Ht 70 in T 98.6°F BP 115/68 sitting 115/65 standing HR 78 RR 18

PSA 4.1

All other labs were within normal limits.

His physician asks your opinion about this patient's medication therapy options. He would like to reserve the use of levodopa/carbidopa until the patient's symptoms worsen, and would like an acceptable alternative.

What other class of medications would be most effective to begin at this time?

A. dopamine agonists
B. anticholinergic agents
C. COMT inhibitor
D. antioxidants

Dopamine Agonists	Bromocriptine, pramipexole, ropinirole, apomorphine
Mechanism of Action	Direct stimulation of postsynaptic dopamine receptors increasing dopamine activity in the brain
***Contraindications*/ Precautions**	*Hypersensitivity*/Orthostatic hypotension, dyskinesias, hallucinations, impulse control disorders, pleural/retroperitoneal fibrosis, retinal changes, somnolence, renal impairment, melanoma, hepatic impairment, CYP3A4 inhibitor use (bromocriptine), uncontrolled hypertension, severe ischemic heart disease, pregnancy, peripheral vascular disorders, 5-HT_3 antagonists
Adverse Effects	Nausea, dizziness, somnolence, insomnia, constipation, asthenia, hallucinations, orthostatic hypotension, angina, falls, edema
Drug Interactions	CNS depressants, MAO inhibitors, atypical antipsychotics, cimetidine, methylphenidate, CYP1A2 substrate (ropinirole), 5-HT_3 antagonists, dronedarone, quinidine, ciprofloxacin, CYP3A4 substrate (bromocriptine)
Monitoring	Efficacy, daytime somnolence, blood pressure, heart rate, body weight, dyskinesias, CNS depression, fall risk, hepatic and renal function
Case Notes	Dopamine agonists are a good monotherapy option for patients younger than 65 years of age with mild-to-moderate symptoms of Parkinson's disease. The use of these agents early in the disease process may reserve the use of levodopa/carbidopa to later in the disease. This may also limit the risk of motor symptom adverse effects that develop with levodopa/carbidopa use. In younger patients who may live with the disease for a longer time, this may be preferable. Anticholinergic agents may be used in the treatment of tremor in Parkinson's disease, but in this patient, they may worsen his BPH. COMT inhibitors are best used with levodopa therapy to increase the amount of levodopa available to cross the blood-brain barrier. Antioxidants like vitamin E have been used in Parkinson's disease, but efficacy data are lacking at this time. One dopamine agonist, apomorphine, is an injectable product reserved for treatment of "off" episodes.

A 58-year-old with Parkinson's disease presents to his primary care provider with complaints of worsening symptoms. His tremor is now affecting both hands, he feels unsteady at times, and he has difficulty starting and stopping when walking. On examination, his additional symptoms of cogwheel rigidity, bradykinesia, blurred vision, and blank facial expression have also become more pronounced. His medical history includes benign prostatic hypertrophy and osteoarthritis. His symptoms have started to affect his ability to perform his activities of daily living and his work performance.

Allergies: NKDA

Medications: Acetaminophen 1,000 mg tablet (OTC) 1 po twice daily; multivitamin tablet (OTC) 1 po daily; finasteride 5 mg tablet 1 po daily; pramipexole 4.5 mg ER tablet 1 po daily

Physical Exam/Other Studies:

Wt 192 lb Ht 70 in T 98.6°F BP 110/68 sitting 108/64 standing HR 78 RR 18

PSA 4.5

All other labs were within normal limits.

What medication should be added at this time to improve his motor symptoms?

Carbidopa/Levodopa	Decarboxylase inhibitor/dopamine precursor
Mechanism of Action	Levodopa is converted to dopamine once it crosses the blood-brain barrier thus increasing dopamine levels in the brain. Carbidopa prevents the peripheral conversion of levodopa to dopamine before it crosses the blood-brain barrier.
***Contraindications*/ Precautions**	*Hypersensitivity, narrow-angle glaucoma, MAO inhibitor use (unless MAO type B), history of melanoma*/ Dyskinesia, orthostatic hypotension, melanoma, psychiatric disorders, cardiovascular disease, renal disease, hepatic disease, peptic ulcer disease, respiratory disease
Adverse Effects	Nausea, vomiting, anorexia, orthostatic hypotension, cardiac arrhythmias, confusion, agitation, hallucinations, dyskinesias, "wearing off" and "on off" phenomena
Drug Interactions	Antipsychotics, MAO inhibitors (unless MAO type B), methionine, methylphenidate, metoclopramide, phenytoin, pyridoxine, high-protein diets, alcohol
Monitoring	Efficacy, dyskinesias, mental status changes, blood pressure (sitting and supine)
Case Notes	Levodopa/carbidopa is the most effective anti-Parkinson's agent. Carbidopa does not cross the blood-brain barrier. Combining levodopa with carbidopa inhibits the conversion of levodopa until it crosses the blood-brain barrier. A total of 75 mg/day of carbidopa is usually required to inhibit peripheral dopa decarboxylase activity. This allows for lower doses of levodopa to be used, which helps to decrease nausea and vomiting that occurs with the use of levodopa. Nearly all patients will need to be on this therapy at some point in their disease. Levodopa/carbidopa use is limited by undesirable adverse effects including movement disorders that occur in up to 55% of patients within the first six months of use. These movement disorders may be reduced by adding dopamine agonists or COMT inhibitors or decreasing the dose or dosing frequency of levodopa. Carbidopa/levodopa is available as an immediate-release product and a controlled-release product. No more than eight tablets per day should be used of either product.

A 42-year-old woman is in the hospital after a motor vehicle accident. She developed peritonitis one week ago and was started on parenteral nutrition (PN) five days ago. Her past medical history is significant for multiple urinary tract infections.

Allergies: Sulfa (rash)

Medications: Piperacillin/tazobactam 3.375 g intravenous every six hours; hydrocodone/acetaminophen 7.5/325 mg tablet 2 po every six hours
PN containing:
Total volume 2,000 mL Dextrose 15% Standard amino acids 80 g
Lipid emulsion (20%) 400 mL
NaCl 70 mEq KPhos 90 mEq CaGluconate 20 mEq Mg 15 mEq Adult MVI 10 mL
Chromium 15 mcg Copper 0.4 mg Manganese 100 mcg Selenium 20 mcg Zinc 5 mg
Ranitidine 300 mg

Physical Exam/Other Studies:
Wt 163 lb Ht 64 in BP 131/72 HR 79 RR 13
Chemistry: Na 128 K 4 Cl 100 CO_2 30 BUN 32 SCr 2.2 Glucose 105 AST 27
ALT 34 AlkPhos 112 Tbili 0.3 TG 220

Her serum creatinine was 1.1 before PN was started and has since increased to 2.2. Which macronutrient of the PN should be decreased based on this patient's current renal function?

Amino Acid	Standard amino acid solutions and specialized mixtures
Mechanism of Action	Intravenous amino acids provide nutrients essential for normal function of cell membranes.
***Contraindications*/ Precautions**	Impaired renal or hepatic function
Adverse Effects	Proteinuria, metabolic acidosis in the presence of renal dysfunction
Drug Interactions	None
Monitoring	BUN, SCr, ammonia (long-term)
Case Notes	Protein needs are decreased in the presence of renal impairment, and higher doses may exceed the kidneys' ability to eliminate protein. This patient's amino acids should be decreased by half, then titrated up to 0.8 g/kg/day, if tolerated. Standard amino acid solutions contain essential and nonessential amino acids. There is a specialty amino acid mixture containing histidine and only essential amino acids for patients with renal dysfunction who do not tolerate standard amino acid solutions. A product is available for those with hepatic disease that contains a higher percentage of branched-chain amino acids and a lower percentage of aromatic amino acids. Specialty products are also available for neonates and young children that contain additional amino acids and have a lower pH, which may be needed to ensure compatibility of higher doses of calcium and phosphorous. Consideration should also be given to eliminating selenium from the TPN.

A 2-year-old girl has been receiving total parenteral nutrition (TPN) for two months due to short bowel syndrome. She is in the hospital following an automobile accident where she suffered abdominal trauma requiring removal of a large portion of the small intestine.

Allergies: Amoxicillin (hives)

Medications: TPN with macronutrients, electrolytes, trace elements, pediatric multivitamin, lipids

Physical Exam/Other Studies:

Physical exam reveals no pertinent findings.

Chemistry: Na 132 K 4.2 Cl 102 CO_2 24 BUN 16 Cr 0.6 Glucose 123

Ca 9.2 Mg 1.7 Phos 4.2 AST 52 ALT 64 Direct bilirubin 2.2 Trig 240

Based on this patient's direct bilirubin of 2.2, there are two trace elements that should be removed from her TPN. One of them is manganese. What is the other trace element that should be removed?

Copper	Trace element (chromium, copper, iodide, manganese, selenium, zinc)
Mechanism of Action	Helps maintain normal red and white cell formation by serving as a cofactor for iron metabolism
***Contraindications*/Precautions**	*Hypersensitivity, Wilson's disease*/Biliary obstruction
Adverse Effects	Behavioral changes, diarrhea, marasmus, hypotonia, photophobia, hepatic dysfunction, peripheral edema
Drug Interactions	Molybdenum increases copper excretion
Monitoring	Bilirubin
Case Notes	Trace elements are essential components of total parenteral nutrition and are typically supplied as a combination product containing four (chromium, copper, manganese, zinc) or five (chromium, copper, manganese, selenium, zinc) of the trace minerals. When the bilirubin is ≥2, copper and manganese may begin to accumulate, causing further hepatotoxicity and other effects listed above. Those must be removed from the TPN and the other trace elements added to the TPN individually rather than using a combination product. Signs of copper deficiency include neutropenia, leukopenia, osteoporosis, dermatitis, diarrhea, mental deterioration, and hypercholesterolemia.

A 2-month-old is receiving parenteral nutrition (PN) secondary to abdominal surgery. He started PN one week ago and has tolerated it without problems. He has no other medical conditions.

Allergies: NKDA

Medications:

PN containing:
Total volume 360 mL Dextrose 14% Standard amino acids 5 g
Lipid emulsion (20%) 20 mL
NaCl 15 mEq KPhos 10 mEq CaGluconate 9 mEq Mg 1.4 mEq Pediatric MVI 5 mL
Chromium 0.7 mcg Copper 72 mcg Iodide 3.5 mcg Manganese 3.5 mcg Selenium 8 mcg
Zinc 1 mg Ranitidine 20 mg

Physical Exam/Other Studies:

Wt 8 lb Ht 21 in BP 92/54 HR 140 RR 26
Physical exam reveals no pertinent findings
Chemistry: Na 141 K 5.2 Cl 98 CO_2 27 BUN 14 Cr 0.2 Glucose 97 AST 22
ALT 31 AlkPhos 324 Tbili 0.3 TG 124

Which ingredient of this PN necessitates the use of a central line rather than a peripheral line?

Dextrose	Intravenous nutritional therapy
Mechanism of Action	Source of calories and fluid
***Contraindications*/Precautions**	*Hypersensitivity to corn*/Premature infants (start with low infusion rates), diabetes
Adverse Effects	With excessive infusion rates: Venous thrombosis, edema, dehydration, confusion, hyperglycemia, hypokalemia, hypophosphatemia, hypomagnesemia, pulmonary edema
Drug Interactions	None known
Monitoring	Blood and urine glucose, serum electrolytes
Case Notes	The maximum recommended dextrose concentration in a peripheral line is 12.5%. Higher concentrations delivered peripherally increase the risk for thrombosis, necessitating administration via a central line. In emergency situations, up to 25% can be given peripherally but is generally not recommended. The initial dextrose concentration should not exceed 10-12.5% (or 9 mg/kg/min) and is titrated daily up to the goal concentration to meet caloric needs. Maximum recommended concentrations and dextrose administration rates are dictated by patient age. Each gram of dextrose contains 3.4 Kcal.

A 7-year-old girl is receiving parenteral nutrition (PN) secondary to abdominal trauma. She started PN two weeks ago and has tolerated it without problems.

Allergies: Penicillin (hives)

Medications:

Daily PN containing:
Total volume 1,500 mL Dextrose 15% Standard amino acids 50 g
Lipid emulsion (20%) 200 mL
NaCl 60 mEq KPhos 50 mEq CaGluconate 30 mEq Mg 8 mEq Pediatric MVI 5 mL
Chromium 10 mcg Copper 0.35 mg Iodide 20 mcg Manganese 80 mcg Selenium 40 mcg
Zinc 5 mg Ranitidine 100 mg

Physical Exam/Other Studies:

Wt 44 lb Ht 48 in BP 100/68 HR 86 RR 12
Physical exam reveals no pertinent findings.
Chemistry: Na 131 K 3.6 Cl 110 CO_2 25 BUN 11 Cr 0.4 Glucose 105 AST 27
ALT 34 AlkPhos 351 Tbili 0.9 TG 180

Which ingredient of this PN is providing 400 calories per day?

Fat Emulsion	10%, 20%
Mechanism of Action	Intravenous fat emulsions provide calories essential for normal function of cell membranes.
***Contraindications*/ Precautions**	*Hypersensitivity to fat emulsion, egg, soybean; pancreatitis with hyperlipidemia; lipoid nephrosis*/Severe liver damage, pulmonary disease, coagulation disorders, cholestasis
Adverse Effects	Hypercoagulability, thrombocytopenia (neonates), leukopenia, hyperlipidemia, jaundice, cholestasis, increased liver enzymes, sepsis, dyspnea
Drug Interactions	Heparin added to solution should not exceed 2 units/mL.
Monitoring	Serum triglycerides, platelets (neonates), liver enzymes, bilirubin
Case Notes	Intravenous fat emulsions contain 10 Kcal/g. A 20% solution contains 20 g/100 mL, which is 200 Kcal/100 mL, which is the same as 2 Kcal/mL. This patient is receiving 200 mL (or 40 g) for a total of 400 calories per day. Lipid calories should generally supply 40% of daily calories and not exceed 60%. For a child of this age, lipids should not exceed 3 g/kg/day. Triglycerides and bilirubin should be checked before starting, after each dosage change, and then weekly after final PN is established. Only 20% fat emulsions should be used in neonates to prevent accumulation of fat in the plasma. Dextrose contains 3.4 Kcal/g, and amino acids provide 4 Kcal/g.

An 83-year-old woman presents to the pharmacy seeking advice about a rash on her face. The rash is present around her nose and mouth and has been there for approximately one month. The rash does itch but is not painful. When asked if it interferes with her ability to eat, she states that she doesn't eat much anyway because nothing tastes good to her. Her past medical history is significant for hypertension.

Allergies: NKDA

Medications: Aspirin 81 mg tablet (OTC) 1 po once a day; amiloride/hydrochlorothiazide 5/50 mg tablet 1 po once a day

Physical Exam/Other Studies:

Wt 115 lb Ht 66 in BP 121/74 HR 67 RR 15

Physical exam reveals moist erythematous rash in both nasolabial folds and at the creases of her mouth.

Which of the following nutrient deficiencies would cause her symptoms of rash and impaired taste?

A. iron
B. zinc
C. chromium
D. ascorbic acid

Zinc	Trace element (capsule, lozenge, tablet, or injection)
Mechanism of Action	A cofactor for enzymes essential to carbohydrate and protein metabolism. Maintains tissue repair, skin hydration, and sense of smell and taste.
***Contraindications*/ Precautions**	Administration without copper may decrease copper levels.
Adverse Effects	Indigestion, sweating. With excessive doses, hypothermia, blurred vision, or jaundice may occur.
Drug Interactions	Coffee, legumes, whole-grain cereals, bran, and dairy reduce zinc absorption.
Monitoring	Copper and zinc levels, alkaline phosphatase
Case Notes	This patient's symptoms are consistent with zinc deficiency. The elderly are at risk for zinc deficiencies due to poor nutrition and changes in gastric pH. Other symptoms of zinc deficiency may include alopecia, diarrhea, depression, and impaired wound healing. The recommended dose to treat a deficiency is 25-50 mg elemental zinc (110-220 mg zinc sulfate) three times per day. Clinical response may take six to eight weeks. Serum levels may be obtained but do not reflect total body zinc. Zinc is supplied as a capsule, lozenge, tablet, and solution for injection.

A 40-year-old woman presents to your clinic with a chief complaint of frustration due to lack of success with diet and exercise-driven weight loss program. She has been obese for the past three years and is looking for a prescription medication that may help her lose weight. She currently does cardiovascular exercises such as walking and jogging for 30 minutes every day and has done her best to incorporate better food choices into her diet. These two activities have not given her the weight loss success she is seeking. She has been diagnosed with diabetes, dyslipidemia, and hypertension.

Allergies: NKDA

Medications: Glyburide 10 mg tablet 1 po every morning and evening; metformin 500 mg tablet 1 po every morning and evening; lovastatin 20 mg tablet 1 po every evening; aspirin 81 mg tablet (OTC) 1 po every morning; captopril/hydrochlorothiazide 25/25 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 260 lb Ht 69 in BMI 38.4 kg/m^2 BP 138/88 HR 86 Fasting glucose 128
Physical exam reveals no pertinent findings.

What medication would be the most effective at helping her lose weight when combined with her diet and exercise routine?

Orlistat	Lipase inhibitor
Mechanism of Action	A reversible inhibitor of gastric and pancreatic lipases, thus inhibiting absorption of dietary fats
***Contraindications*/ Precautions**	*Hypersensitivity, chronic malabsorption syndrome or cholestasis*/Cholelithiasis, hepatotoxicity, increased urinary oxalate, diabetes
Adverse Effects	Headache, oily spotting, abdominal pain/discomfort, flatus with discharge, fecal urgency, fatty/oily stool, oily evacuation, defecation increased, back pain, upper respiratory infection, influenza. Gastrointestinal side effects decrease in frequency over time.
Drug Interactions	Amiodarone absorption may be decreased with orlistat. Cyclosporine, levothyroxine, and fat-soluble vitamin concentrations may be decreased when administered with orlistat. Separate medications by two hours. Orlistat may enhance the anticoagulant effect of warfarin.
Monitoring	BMI, diet (calorie and fat intake), serum glucose in patients with diabetes, thyroid function in patients with thyroid disease, liver function tests in patients exhibiting symptoms of hepatic dysfunction, cyclosporine levels closely if taking cyclosporine
Case Notes	Orlistat has shown an increase in the amount of weight lost and a decrease in the amount of weight regained during weight loss programs. Orlistat can result in a weight loss of approximately 2-4 kg when adding it to diet. Approximately 80% of patients will initially experience at least one gastrointestinal side effect from orlistat. The side effects are most common in the first two months, but will improve with continued use. Fat-soluble vitamin supplementation is recommended at least two hours before or after orlistat dose. Prescription dosage for orlistat is 120 mg po three times daily with each main meal. Over-the-counter orlistat dose is 60 mg po three times daily with each main meal. If a patient misses the meal regularly or the meal does not contain fat, the dose should be omitted. FDA issued a warning for the prescription and OTC therapy concerning severe liver injury with this medication. Caution should be exercised when recommending it.

A 67-year-old woman presents to your community pharmacy complaining of joint pain uncontrolled by topical over-the-counter agents. She has a history of hypertension, dyslipidemia, and osteoporosis. She states she does not have a history of liver or kidney disease. She states her pain is more intense upon awakening every morning and subsides by the end of the day. The pain is localized in her joints, but sometimes she has muscle pain as well. She describes the pain as 3 out of 10 on most days. She has a family history of heart disease, dyslipidemia, osteoporosis, and arthritis. She lives at home with her husband, is retired, and enjoys playing golf on the weekends. She does not use tobacco products or illicit drugs, but does enjoy a glass of white wine with her lunch and dinner meals five days out of each week.

Allergies: Codeine (rash), eggs (hives)

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; lisinopril 10 mg tablet 1 po daily; alendronate 70 mg tablet 1 po weekly; atorvastatin 10 mg tablet 1 po every evening; methyl salicylate and menthol topical cream (OTC) applied to affected areas three times daily

Physical Exam/Other Studies:

Wt 262 lb Ht 70 in BP 132/78 HR 62

What over-the-counter pain management medication is most appropriate for this patient considering her symptoms and history?

Acetaminophen	Para-aminophenol
Mechanism of Action	Inhibits the synthesis of prostaglandins in the central nervous system and peripherally blocks pain impulse generation; produces antipyresis from inhibition of hypothalamic heat-regulating center
***Contraindications*/ Precautions**	*Hypersensitivity to acetaminophen or any component of the formulation/*Hepatotoxicity, ethanol use, G6PD deficiency
Adverse Effects	Rash, electrolyte disturbances, anemia, hepatic enzyme disturbances, hepatotoxicity and nephrotoxicity with chronic use
Drug Interactions	Monitor therapy in combination with hydantoin, barbiturates, carbamazepine, cholestyramine resin, conivaptan, imatinib, isoniazid, peginterferon alfa-2b, vitamin K antagonists, ethanol
Monitoring	Relief of pain or fever, liver function enzymes with chronic daily use
Case Notes	Acetaminophen is first-line treatment of osteoarthritis (OA) due to the severity of this patient's condition. Discuss with her the importance of taking it exactly how it is recommended (325-1,000 mg po or per rectum every four to six hours; no more than 4 g/day) and not increasing dose or frequency. In patients who are elderly, have chronic alcoholism, or liver disease, a limit of less than 2 g/day is needed. She does not have a history of liver disease or alcoholism, but education regarding alcohol intake is warranted in this patient. Discuss the importance of limiting her ethanol intake to three drinks per day maximum. The tolerance of the medication can be improved by taking it with food or milk. Avoid other prescription or over-the-counter medications that contain acetaminophen. Because of this patient's weight, she may benefit from weight loss to help decrease the load on her weight-bearing joints. If acetaminophen is ineffective at relieving symptoms of OA, NSAIDs are second-line therapy.

A 60-year-old woman presents to the pharmacy in need of advice. She tells you she recently got a fever and has been experiencing myalgias in her lower back that are bothersome to her. She has a past medical history of hypertension, diabetes, and a myocardial infarction approximately three years ago. She is looking for something to help with her symptoms, but because of her recent MI, she does not know what over-the-counter medication to choose.

Allergies: NKDA

Medications: Atenolol 25 mg tablet 1 po twice daily; nitroglycerin 0.4 mg sublingual tablet 1 sublingually at onset of chest pain and every five minutes thereafter; metformin extended release 500 mg tablet 1 po twice daily; pravastatin 40 mg tablet 1 po at bedtime

Physical Exam/Other Studies:

Wt 150 lb Ht 66 in T 101.1° F BP 128/80 HR 80 RR 18

What is the best recommendation for this patient's current symptoms?

Acetylsalicylic Acid (ASA)	Salicylates (acetylsalicylic acid [aspirin], magnesium-anhydrous, diflunisal)
Mechanism of Action	Prevents the formation of prostaglandins produced in response to noxious stimuli, thereby decreasing the number of pain impulses received by the CNS
***Contraindications*/ Precautions**	*Hypersensitivity to salicylates, other NSAIDs, or any component of the formulation, asthma, rhinitis, nasal polyps, inherited or acquired bleeding disorders, children younger than 16 years for viral infections with or without fever due to potential Reye's syndrome, pregnancy*/Salicylate sensitivity, tinnitus, upper GI events, bleeding disorders, dehydration, ethanol, GI disease, hepatic impairment, renal impairment, concurrent use with alteplase, COX-2 inhibitors, NSAIDs
Adverse Effects	Hypotension, edema, rash, angioedema, nausea, vomiting, dyspepsia, epigastric pain, heartburn, stomach pain, GI ulcers, gastric erosions, prolonged prothrombin times, hepatotoxicity, LFT elevations, hepatitis, rhabdomyolysis, hearing loss, tinnitus, interstitial nephritis, bronchospasm, asthma, dyspnea, anaphylaxis, Reye's syndrome, and many others. Refer to product information for more adverse effects.
Drug Interactions	Avoid concomitant use with ketorolac; increased effect with anticoagulants, corticosteroids, heparin, vitamin K antagonists, antiplatelet agents, ginkgo biloba, ketorolac, NSAIDs, pentoxifylline, SSRI, ethanol. Many other drug interactions exist. Refer to product information for specific interactions.
Monitoring	Allergic reactions, bleeding events, resolution of symptoms
Case Notes	Acetylsalicylic acid has many uses: treatment of mild to moderate pain, inflammation, and fever; prevention/treatment of MI, acute ischemic stroke, and transient ischemic episodes; management of rheumatoid arthritis, rheumatic fever, osteoarthritis, and gout; adjunctive therapy in revascularization procedures; and stent implantation. In this patient, not only can it treat her pain, inflammation, and fever, but it is also indicated to help prevent MI because of her increased risk from her diabetes diagnosis and past history of MI. Dosing for fever/inflammation/pain is 325-1,000 mg po every four to six hours (maximum 4,000 mg/day) and for MI prevention is 81 mg/day.

A 23-year-old woman presents to your pharmacy counter complaining of menstrual pain, cramping, and headache that has been going on for the last 12 hours. She has a history of such pains during each cycle, usually controlled by nonpharmacologic treatments until this month. She says she is supposed to start her cycle in the next day. She has no active gastrointestinal disease, bleeding disorder or history of ovarian cysts. Her cycles are regulated by birth control pills. She is looking for something over-the-counter that she can use to help treat her cramps.

Allergies: Amoxicillin (rash)

Medications: Ethinyl estradiol and norgestimate triphasic tablets 1 po daily on days 1-21

Physical Exam/Other Studies:

Wt 112 lb Ht 62 in T 98.4° F BP 118/72 HR 66 RR 16

You correctly identify that this patient is having signs and symptoms of primary dysmenorrhea and she would like your advice to gain relief.

What class of medications should you recommend for her today?

Nonsalicylate Nonsteroidal Anti-inflammatory Drugs	Ibuprofen, naproxen, naproxen sodium, fenoprofen, ketoprofen
Mechanism of Action	Reversible inhibition of cyclooxygenase-1 and -2 (COX-1 and -2) enzymes, resulting in decreased formation of prostaglandin precursors. This class has antipyretic, analgesic, and anti-inflammatory properties.
***Contraindications*/ Precautions**	*Hypersensitivity, history of asthma, urticaria, or allergic-type reaction to aspirin or other NSAIDs, aspirin triad (eg, asthma, aspirin intolerance, nasal polyps)*/Increased risk of adverse cardiovascular thrombotic events, including fatal MI and stroke, increased risk of gastrointestinal irritation, inflammation, ulceration, bleeding, and perforation, platelet adhesion and aggregation may be decreased, may prolong bleeding time, renal impairment, hypertension
Adverse Effects	Edema, dizziness, headache, rash, itching, gastrointestinal effects, tinnitus, fluid retention
Drug Interactions	Absorption decreased by bile acid sequestrants; nephrotoxic effects enhanced with cyclosporine; bleeding effects enhanced with drotrecogin alfa, alfalfa, anise, bilberry, salicylates, SSRI, warfarin; increased serum concentrations of lithium, methotrexate, pemetrexed
Monitoring	CBC, chemistry profile, periodic liver function, renal function (serum BUN, creatinine)
Case Notes	Primary dysmenorrhea is a result of increasing prostaglandin levels at the end of the luteal phase. First-line treatment is a nonsalicylate NSAID. The prescriber should be consulted before use if the patient has hypertension or heart failure. Do not take longer than three days for fever, or 10 days for pain without consulting a medical advisor. Adverse reactions can occur with overuse. This drug should not be used in the third trimester of pregnancy. The two most common nonsalicylate NSAIDs are ibuprofen and naproxen. OTC dosing for ibuprofen is 200-400 mg every four to six hours (maximum: 1,200 mg/day). OTC naproxen dosing is 220-440 mg initially, then 220 mg every 8-12 hours (maximum: 660 mg/day). Rx maximum doses are 3,200 mg/day and 1,250 mg/day, respectively.

A 41-year-old man presents to the pharmacy in apparent distress. He states that he has been controlled on his current seizure medications for the past 10 years and had his first seizure in three years last night. He wanted to talk to you first because his doctor is not in the office today because it is a weekend. He was recently prescribed a new medication for pain but is unsure what the name of it is. He states, "I just take what my doctor tells me and don't ask questions." He has a past medical history of seizures, chronic back pain, generalized anxiety disorder, and hypertension.

Allergies: Morphine (hives)

Medications: Topiramate 100 mg tablet 1 po twice daily; tramadol 50 mg tablet 1 po every 6 hours PRN; sertraline 50 mg tablet 1 po daily; hydrochlorothiazide 25 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 167 lb Ht 65 in BP 146/88 HR 90

This patient had a seizure because one of his medications lowered his seizure threshold. What medication is most likely responsible and should be discontinued?

Tramadol	Central analgesic
Mechanism of Action	Binds to the mu-opiate receptors in the CNS causing inhibition of ascending pain pathways, altering the perception of and response to pain; also inhibits the reuptake of norepinephrine and serotonin, modifying the ascending pathway
***Contraindications*/ Precautions**	*Hypersensitivity to tramadol, opioids, or a component of the formulation, opioid-dependent patients, acute intoxication with alcohol, hypnotics, centrally acting analgesics, opioids, or psychotropic drugs*/ Anaphylactoid reactions, CNS depression, seizures, abdominal conditions, drug abuse, ethanol use, head trauma, hepatic and/or renal impairment, respiratory disease, suicide risk, serotonin syndrome
Adverse Effects	Flushing, dizziness, headache, somnolence, insomnia, pruritus, constipation, nausea, vomiting, dyspepsia, weakness
Drug Interactions	Major substrate of CYP2D6, 3A4
Monitoring	Pain relief, RR, BP, HR, and signs of tolerance or abuse
Case Notes	Tramadol, either alone or in combination with a serotonin reuptake inhibitor, has the potential to reduce the seizure threshold in a patient with a seizure disorder. It should be discontinued in this patient. The concern of serotonin syndrome also exists with this combination of tramadol plus an SSRI. Tramadol is indicated for relief of moderate to moderately severe pain. Dosage for tramadol is 50-100 mg every four to six hours. Dosage limits for extended-release formulations is 300 mg/day, and the immediate-release formulation limit is 400 mg/day. Use is not recommended in patients with hepatic impairment. Patients with Clcr <30 mL/min should only take two tablets every 12 hours for no more than five days. Combination products exist that contain tramadol (37.5 mg) and acetaminophen (325 mg). Be cautious of acetaminophen dosage ceiling of no more than 4,000 mg/day when using this combination.

A 40-year-old man presents to your internal medicine service after being involved in a construction accident. He suffered severe lacerations to the hand and is in severe pain. He has a history of diabetes, hypertension, dyslipidemia, and chronic back pain from a previous car accident 10 years ago, successfully treated with hydrocodone/acetaminophen. He smokes one pack/day for 11 years, does not drink alcohol, and lives at home with his wife and 4-year-old daughter.

Allergies: NKDA

Medications: Hydrocodone/acetaminophen 5/500 mg tablet 1 po every six hours PRN pain (needs approximately 1 tablet at bedtime); glipizide extended release 10 mg tablet 1 po every morning; pioglitazone 15 mg tablet 1 po every morning; enalapril 10 mg tablet 1 po every morning; atorvastatin 20 mg tablet 1 po at bedtime

Physical Exam/Other Studies:

Wt 210 lb Ht 66 in T 97.1° F BP 146/82 HR 86 RR 19 O_2 sat 99%
Na 137 K 4.0 Cl 101 random glucose 194 SCr 1.3 Pain 7 out of 10

You are asked to select a pain medication most appropriate for this patient.

Based on his history and severe pain level, what class of medications would be the best choice for this patient?

Opioid Analgesic (Phenanthrene)	Morphine, hydromorphone, oxymorphone, levorphanol, codeine, hydrocodone, oxycodone
Mechanism of Action	Binds to opiate receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain; produces generalized CNS depression
***Contraindications/* Precautions**	*Hypersensitivity, significant respiratory depression, hypercarbia, acute or severe asthma, pregnancy (prolonged use or high doses at term)/*Abuse potential, CNS depression, may cause hypotension, phenanthrene hypersensitivity; for complete list, see drug monograph
Adverse Effects	Somnolence, dizziness, pruritus, nausea, constipation, vomiting, postural hypotension, CNS effects, xerostomia, weakness, diaphoresis, hiccups, twitching, abdominal pain, and others
Drug Interactions	May enhance the adverse effect of alvimopan in patients receiving long-term opiates prior to alvimopan initiation; mixed agonist/antagonist opioids may diminish the analgesic effect of opioids; ethanol may increase CNS depression; oxycodone is a substrate of CYP3A4 isoenzyme and interacts with 3A4 inducers, inhibitors
Monitoring	Pain relief, respiratory and mental status, and blood pressure
Case Notes	Phenanthrene opiates are most appropriate for this patient because they are indicated for moderate to severe pain. When converting from opiate to opiate, remember to use equianalgesic dosing principles, or morphine conversion rates, to ensure the patient receives the proper dose of opiates to control pain. Options for treatment include combination products with NSAIDs, acetaminophen, or aspirin, controlled-release tablets or capsules, or immediate-release tablets or capsules for breakthrough pain. Opiates not in combination with NSAIDs, acetaminophen, or aspirin do not have dose ceilings and are typically preferred in patients with chronic pain. Dependence is a possibility with these therapies, so caution must be taken. In patients with unstable angina/non-ST segment elevation MI, morphine is recommended when NTG does not provide relief or acute pulmonary edema and/or agitation is present.

A 38-year-old woman presents to the hospital complaining of severe pain associated with a motorcycle wreck. Severe lacerations to the right leg and arm are visible, and based on this patient's presentation, you know the physician will ask your recommendation on an appropriate pain medication. She has a history of diabetes, hypertension, allergic rhinitis, acute myocardial infarction, seizures, COPD, and dyslipidemia. She reports a history of smoking one pack/day for 15 years and drinks two to three alcoholic beverages approximately once a week.

Allergies: Tramadol (rash)

Medications: Metformin 500 mg tablet 1 po twice daily with food; hydrochlorothiazide 25 mg tablet 1 po daily; loratadine 10 mg tablet (OTC) 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; carbamazepine 200 mg tablet 1 po twice daily; albuterol inhaler 1-2 puffs by mouth every four to six hours PRN SOB; ipratropium inhaler 2 puffs po four times daily; pravastatin 20 mg tablet 1 po at bedtime

Physical Exam/Other Studies:

Wt 180 lb Ht 68 in T 96.5° F BP 144/86 HR 96 RR 19 O_2sat 98%

Physical exam reveals severe lacerations on the right arm and leg, pain scoring 8 on a scale of 1 to 10, and labored breathing consistent with a COPD exacerbation.

Labs are being processed and are unavailable at this time.

All of the following are appropriate pain medication selections except _____.

A. oxycodone
B. meperidine
C. morphine
D. hydrocodone

Meperidine	Phenylpiperidines (meperidine, fentanyl)
Mechanism of Action	Binds to opiate receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain; produces generalized CNS depression
***Contraindications*/ Precautions**	*Hypersensitivity, use with or within 14 days of MAO inhibitors, pregnancy (prolonged use or high doses near term)*/CNS depression, CNS events (seizures, anxiety, tremors), hypotension, adrenal insufficiency, biliary tract impairment, drug abuse, head trauma, hepatic impairment, respiratory disease, thyroid dysfunction
Adverse Effects	Hypotension, seizure, drowsiness, dizziness, nervousness, urticaria, nausea, vomiting, dyspnea. Please see product information for complete list.
Drug Interactions	Major substrate of CYP3A4; increases levels of alcohol, CNS depressants, SSRI, thiazides; meperidine levels increased by amphetamines, antipsychotic agents, barbiturates, MAO inhibitors, protease inhibitors, avoid valerian, St John's wort, kava kava, gotu kola
Monitoring	Pain relief, respiratory and mental status, BP, excessive sedation, CNS depression, seizures
Case Notes	Meperidine is not appropriate for this patient based on her history of seizures and COPD, both of which are conditions that meperidine can exacerbate. This medication was identified as a high-alert medication, and its use is not recommended for pain control, especially in elderly and renally compromised patients because of the risk of neurotoxicity. Meperidine dosing: 50-75 mcg IM or SC every three to four hours; 5-10 mg IV every five minutes PRN; 50 mg po every three to four hours PRN. Fentanyl is a phenylpiperidine also, and is used for pre- and postoperative pain (IV), chronic pain (transdermal), and breakthrough cancer pain in opioid-tolerant patients (transmucosal). See specific dose conversion guidelines for patients on opiates being started on fentanyl. Patients on fentanyl patches should not be converted back to opioids using the same tables. They should be retitrated up to the most effective dose. See product information for fentanyl boxed warnings.

A 31-year-old woman presents to your family medicine clinic for a checkup. While present, you find out she has become dependent on opioid pain killers. She states she no longer wants to be dependent on them but is having trouble getting off of them. She is seeking your advice as a pharmacist on any safe medications that will help slowly taper her off morphine. She was prescribed morphine after a surgery two months ago and has been taking more morphine than was prescribed every day since the event. She has a past medical history of neuropathic pain in addition to pain s/p surgery.

Allergies: NKDA

Medications: Morphine sulfate controlled release 30 mg tablet 1 po twice daily (taking 2 tablets a day); morphine sulfate immediate release 15 mg tablet 1 po every six hours PRN (taking 10 tablets a day); gabapentin 300 mg tablet 1 po three times daily

Physical Exam/Other Studies:

Wt 132 lb Ht 64 in BP 122/84 HR 78 RR 16

The patient self-identifies that she will need help weaning off of this medication and has decided to check into an opioid treatment facility.

What medication that also has an indication for severe pain can be prescribed for this patient's opioid addiction?

Methadone	Diphenylheptane (methadone, propoxyphene)
Mechanism of Action	Binds to opiate receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain; produces generalized CNS depression
***Contraindications*/Precautions**	*Hypersensitivity, respiratory depression, acute bronchial asthma or hypercarbia, paralytic ileus, concurrent use of selegiline*/QT prolongation, respiratory depression, CNS depression/coma, hypotension, adrenal insufficiency, biliary tract impairment, depression, drug abuse, head trauma, hepatic and/or renal impairment, prostatic hyperplasia/urethral stricture, respiratory disease, thyroid dysfunction
Adverse Effects	Constipation, sweating, sedation, hallucination, cardiovascular effects, GI pain. Please see product information for complete list.
Drug Interactions	Major substrate of CYP2B6, 3A4; moderately inhibits CYP2D6; avoid use with artemether, dronedarone, lumefantrine, nilotinib, pimozide, quinine, thioridazine, ziprasidone
Monitoring	Baseline ECG within 30 days of initiation and annually, relief of pain, RR, BP, mental status
Case Notes	Methadone can be used to help with this patient's opioid dependence. When prescribed for opioid addiction treatment, it should be prescribed by a physician at an opioid treatment facility. In emergency cases, physicians not associated with opioid treatment facilities may prescribe a maximum of three days of methadone treatment for a patient to assist in bridging the gap from physician's office to opioid treatment facility. Methadone is available in oral and IM formulations. It is also effective in severe chronic pain. It may be effective in neuropathic pain as well, which makes it a great choice for this patient who suffers from neuropathy. IM methadone to morphine conversion is 2-to-1. Propoxyphene is also in this drug class and is mainly used for moderate pain. This drug was voluntarily removed from the market due to an increased risk of prolonged PR interval, QRS widening, and prolonged PT interval on electrocardiogram. The FDA concluded that the risks outweigh the benefits and this medication should not be prescribed.

A 54-year-old man presents to your pharmacy with a question regarding his current pain regimen of ibuprofen. He describes his pain as stinging, tingling, shooting pain in his hands that does not improve with topical heat, cold, or the ibuprofen he is currently taking. He says it has been occurring more frequently lately and his current pain regimen is ineffective. He has a past medical history of peripheral vascular disease and hypertension.

Allergies: NKDA

Medications: Simvastatin 40 mg tablet 1 po at bedtime; aspirin 81 mg tablet (OTC) 1 po daily; hydrochlorothiazide 25 mg tablet 1 po daily; ibuprofen 200 mg tablet (OTC) 2 po every six hours PRN

Physical Exam/Other Studies:

Wt 187 lb Ht 71 in BP 146/96 HR 76

He asks if you could recommend something before he goes in to see his doctor.

What is the best medication for this patient's pain?

Gabapentin	Anticonvulsant
Mechanism of Action	Binds to an amino acid carrier protein and appears to act at a unique receptor. Gabapentin inhibits high-voltage-activated calcium channels. It elevates human brain GABA levels, possibly via alterations in GABA synthesis or reversal of the neuronal GABA transporter, resulting in nonvesicular release of GABA.
***Contraindications*/ Precautions**	*Hypersensitivity*/CNS depression, suicidal ideation, renal impairment, sedatives
Adverse Effects	Dizziness, fatigue, somnolence, ataxia, pedal edema, weight gain
Drug Interactions	Cimetidine reduces clearance of gabapentin, aluminum antacids reduce bioavailability; gabapentin levels increased by methotrimeprazine; levels of ethyl alcohol, CNS depressants, methotrimeprazine increased by gabapentin; gabapentin levels decreased by ketorolac, mefloquine; avoid primrose, valerian, St John's wort, kava kava, gotu kola
Monitoring	Serum levels of concomitant anticonvulsant therapy, suicidal ideation
Case Notes	This patient is most likely suffering from peripheral neuropathy secondary to peripheral vascular disease. Gabapentin is commonly used for the treatment of peripheral neuropathy. Its other use is for partial seizures in patients who have failed initial treatment, postherpetic neuralgia, fibromyalgia, postoperative pain, bipolar disorder, social phobia, and vasomotor symptoms. Typical starting dose of gabapentin is 300 mg at bedtime, increasing to 900 mg/day over three days. Maximum dose is 3,600 mg/day; however, recommended dosage range for neuropathy is 300-1,800 mg/day in three divided doses. Due to somnolence, the first dose should be administered at bedtime. In addition to starting gabapentin, this patient should also discontinue his ibuprofen due to his uncontrolled hypertension.

A 30-year-old man presents to your pain management clinic. He was referred by his primary care physician for management of neuropathic pain. He describes the pain as tingling, burning pain in his extremities that did not respond to gabapentin. He has a past medical history of depression, peripheral vascular disease, and diabetes and was recently diagnosed with diabetic neuropathy.

Allergies: Morphine (anaphylaxis)

Medications: Sertraline 50 mg tablet 1 po daily; atorvastatin 20 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; gabapentin 600 mg tablet 1 po twice daily; metformin extended release 1,000 mg tablet 1 po twice daily; pioglitazone 30 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 287 lb Ht 70 in T 98.1° F BP 138/80 HR 80 RR 17

Physical exam reveals decreased sensations in first and fourth toes on the right foot, all toes on the left foot, and both heels. Faint positive bilateral pedal pulses present.

Na 137 K 3.9 SCr 1.0 A1c 8.9% fasting glucose 200

What medication should replace gabapentin for his diabetic neuropathy that may also help treat his depression?

Duloxetine	Serotonin/Norepinephrine reuptake inhibitor (desvenlafaxine, duloxetine, milnacipran, venlafaxine)
Mechanism of Action	Potent inhibitor of neuronal serotonin and norepinephrine reuptake and a weak inhibitor of dopamine reuptake
***Contraindications*/ Precautions**	*Concomitant use or within two weeks of MAO inhibitors, uncontrolled narrow-angle glaucoma/* Suicidal thinking/behavior, bleeding risk, CNS depression, hepatotoxicity, hyperglycemia, orthostatic hypotension/syncope, serotonin syndrome/neuroleptic malignant syndrome—like reactions, sexual dysfunction, SIADH and hyponatremia, urinary hesitancy, HTN, narrow-angle glaucoma, renal impairment, seizure disorders
Adverse Effects	Somnolence, headache, dizziness, insomnia, fatigue, nausea, xerostomia, constipation, diarrhea, appetite decreased
Drug Interactions	Major substrate of CYP1A2, 2D6; use caution with agents that lower seizure threshold or that are anticoagulant/antiplatelet agents
Monitoring	BP, depression symptoms, suicidal ideation, anxiety, social functioning, mania, panic attacks, glucose, A1c, creatinine, BUN, LFT
Case Notes	Duloxetine is the best choice to replace gabapentin for this patient because it has the indications for diabetic neuropathy and for major depressive disorder. It is also used to treat generalized anxiety disorder and fibromyalgia. Dosing for diabetic neuropathy is 60 mg po once daily. Higher doses show no benefit for diabetic neuropathy in clinical trials. Not recommended in patients with hepatic impairment or Clcr <30 mL/min. Duloxetine has no significant activity for muscarinic cholinergic, H_1-histaminergic, or alpha$_2$-adrenergic receptors and does not possess MAO-inhibitory activity.

A 52-year-old man presents to the retail pharmacy with a prescription for metformin. He has recently been diagnosed with diabetes. He smokes two packs/day for 10 years. His diet is poor, consisting of fried, fatty, and high-cholesterol foods. He currently works as a janitor, and states he walks approximately two miles/day when he is at work. He received the pneumococcal polysaccharide vaccine approximately two years ago. In addition to diabetes, he has HTN and seasonal allergic rhinitis. He states that his allergies are uncontrolled at this time, just as they are every fall when the ragweed blooms. He is up to date on all routine vaccinations, including hepatitis A, B, pneuzmococcal, varicella, Tdap, and meningococcal.

Allergies: Codeine (rash)

Medications: Metformin 500 mg tablet 1 po twice daily; hydrochlorothiazide 25 mg tablet 1 po daily; cetirizine 10 mg tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 270 lb Ht 69 in BP 138/82 HR 70

A1c 9.1% fasting glucose 238

What additional vaccination does this patient need?

Trivalent Inactivated Vaccine (TIV)	Seasonal influenza vaccine (trivalent inactivated vaccine [TIV], live attenuated intranasal vaccine [LAIV])
Mechanism of Action	Antigens in the vaccine modulate an immune response, activating antibody production. These antibodies attack, destroy, and eliminate the antigen, producing immunity through memory cells.
***Contraindications*/ Precautions**	*Prior life-threatening reaction to the influenza vaccination, hypersensitivity to any component of the formulation*/Patients with acute illness, a history of bleeding disorders, Guillain-Barré syndrome, HIV, or patients on immunosuppressants
Adverse Effects	Injection site reactions, myalgias, arthralgias
Drug Interactions	Immunosuppressants may diminish the effect of vaccine.
Monitoring	Hypersensitivity, anaphylaxis
Case Notes	This patient is a candidate for the seasonal influenza vaccine. Current ACIP recommendations state that everyone 6 months of age or older should be vaccinated against seasonal influenza, especially those with chronic illnesses such as diabetes and heart disease. The dose for adults is 0.5 cc injected SC in the deltoid muscle one time yearly. The vaccine may cause soreness at the injection site. Protective antibody titers are achieved approximately three weeks post-vaccination. These titers last throughout the influenza season. The influenza vaccine will not give a person the virus. Each product is manufactured differently; therefore, be sure to screen patients for allergies to any of the components of the product being administered. This patient is not a candidate for LAIV because of his age. LAIV is only indicated for those aged 2-49 years.

A 7-year-old boy presents to clinic with his mother in need of his routine vaccinations. He has no current diseases or conditions. He lives with his parents. He just started his fall semester one month ago at a local elementary school, and he also participates in extracurricular activities like kick-ball and youth league basketball. He received all 0-1 year immunizations approximately five years ago. He received a seasonal influenza vaccine injection last year with no side effects. The patient's mother tells you that he is deathly afraid of needles and would prefer if he did not receive any shots today.

Allergies: NKDA

Medications: Acetaminophen 500 mg/5 mL liquid (OTC) 3 mL po every four to six hours PRN (not currently taking)

Physical Exam/Other Studies:

Wt 46 lb Ht 50 in BP 120/80 HR 72 RR 16

What additional vaccination does this patient need?

Live Attenuated Intranasal Vaccine (LAIV)	Seasonal influenza vaccination (live attenuated intranasal vaccine [LAIV], trivalent inactivated vaccine [TIV])
Mechanism of Action	Antigens modulate an immune response, activating antibody production that attacks, destroys, and eliminates the antigen, thus producing immunity through memory cells.
***Contraindications*/ Precautions**	*Prior life-threatening reaction to previous influenza vaccination, hypersensitivity to any component of the formulation, children 2-17 years of age receiving aspirin therapy*/Patients with acute illness, asthma, cardiovascular disorders, diabetes, Guillain-Barré syndrome, hematologic disorders, hepatic disease, HIV, nasal congestion, neurologic/neuromuscular disorders, renal disease, pregnant women, sensitivity to arginine, chicken egg protein, gelatin, or gentamicin
Adverse Effects	Rhinitis, nasal congestion, sore throat, fever
Drug Interactions	Antiviral agents and immune globulins may diminish therapeutic effect of vaccine; immunosuppressants may enhance toxic effect of vaccine; the vaccine may enhance the toxic effect of salicylates, which may result in Reye syndrome; tuberculin test results may be diminished by live vaccine.
Monitoring	Fever, rash
Case Notes	This vaccine is approved for all patients aged 2-49 who do not have any contraindications. This patient is a good candidate for the intranasal vaccine because of his age, aversion to needles, and past medical history of no respiratory conditions such as asthma. LAIV cannot cause influenza because it cannot replicate in the lower respiratory tract due to the temperature of the environment. After LAIV is given, the patient should avoid contact with severely immunocompromised patients for seven days. The dosage differs depending on whether a child has received the vaccine in the past. This child's dose would be 0.1 mL in each nostril each year since he received the influenza vaccine last season.

A 12-year-old girl presents with her mother to the pediatric clinic for her well-child exam. Her past medical history includes Type 1 diabetes, mild intermittent asthma, and allergic rhinitis. She has no complaints today. She lives with her father, goes to school, and participates in after-school activities such as soccer and cheerleading. She states she has lots of friends and makes sure to count her carbohydrates at every meal. Her mother has Type 1 diabetes and dyslipidemia, and her father has hypertension. She reports that she does not drink alcohol, smoke cigarettes, or engage in sexual intercourse. Patient is up to date on her hepatitis B, IPV, MMR, pneumococcal, and varicella series, and received a Tdap vaccine last year, and a flu shot this most recent flu season.

Allergies: NKDA

Medications: Albuterol HFA inhaler 2 puffs by mouth with spacer every four to six hours as needed for shortness of breath or wheezing; loratadine 10 mg tablet (OTC) 1 po every morning PRN; insulin lispro per her insulin pump based on an insulin to carbohydrate ratio of 1:30 and a correction factor of 1:50

Physical Exam/Other Studies:

Wt 80 lb Ht 60 in T 98.0°F BP 106/62 HR 70 RR 14 O_2 sat 97%

Physical exam reveals child in no apparent distress, lungs clear to auscultation, normal breath sounds, no wheezes.

Fasting glucose 120 A1c 7.5% Peak flow 300 (90% of personal best)

Spirometry not performed today.

What vaccine is indicated for this patient today?

Papillomavirus Vaccine (HPV vaccine)	Papillomavirus vaccine types 6, 11, 16, 18; papillomavirus vaccine types 16, 18
Mechanism of Action	Contains inactive HPV proteins that produce neutralizing antibodies to prevent cervical cancer, cervical adenocarcinoma, and cervical, vaginal, and vulvar neoplasia in females, and genital warts caused by HPV in females and males
***Contraindications*/ Precautions**	*Hypersensitivity to papillomavirus recombinant vaccine or any component of the formulation (eg, yeast)/*Moderate or severe acute illness with or without fever, bleeding disorders, active HPV infection, altered immunocompetence, patients younger than 9 years of age, pregnancy
Adverse Effects	Syncope, headache, fever, injection site reactions (pain, erythema, swelling), dizziness, nausea, diarrhea, vomiting, toothache
Drug Interactions	Immunosuppressants
Monitoring	Observe for syncope for 15 minutes after administration of the vaccine. Women require regular gynecologic exams, papillomavirus tests, and cervical cancer screenings after vaccination.
Case Notes	This patient should receive the HPV vaccine to prevent cervical cancer. It is indicated for females aged 9-26 years. The three-dose series should be given at months zero, two, and six for maximum efficacy. Only the papillomavirus vaccine types 6, 11, 16, and 18 will protect against genital warts. Although this patient is not sexually active, the series is still indicated to illicit immunity before sexual activity begins. Because of the risk of syncope, this vaccine should be administered to patients while they are sitting comfortably in a chair, being mindful of objects that could injure the patient in case he/she faints. HPV types 16 and 18 cause 70% of cervical cancers, and types 6 and 11 cause the majority of HPV cases. Once a patient is infected with one HPV vaccine type, the vaccine is no longer effective for that type, but can still convey immunity for the remaining types covered by the vaccine formulation. This vaccine does not protect against pregnancy or HIV.

A 69-year-old woman presents to your pharmacy with a new prescription for atorvastatin and also needs refills of her other chronic medications. Her past medical history includes dyslipidemia, hypertension, osteoporosis, arthritis, and a recent outbreak of shingles that resolved three months ago. She received a flu shot this season and a pneumococcal shot four years ago, is up to date on her hepatitis A and B series, and had a Tdap booster three years ago. She is currently retired, but volunteers in the surgery pre- and postoperation department at the local hospital. She lives with her husband and denies alcohol or tobacco use.

Allergies: NKDA

Medications: Lisinopril 20 mg tablet 1 po daily; amlodipine 5 mg tablet 1 po daily; ibuprofen 600 mg tablet 1 po every six hours PRN; alendronate 70 mg tablet 1 po every week

Physical Exam/Other Studies:

Wt 170 lb Ht 69 in BP 136/76 HR 72

Hip T-score (8 months ago) –2.7

What additional vaccination does this patient need?

Herpes Zoster Vaccine	Live vaccine (herpes zoster, MMR, LAIV, rotavirus, smallpox, varicella, yellow fever)
Mechanism of Action	This live, attenuated vaccine stimulates active immunity to disease caused by the varicella-zoster virus.
***Contraindications*/ Precautions**	*Severe allergic reaction to a component of the vaccine (eg, gelatin, neomycin), immunosuppression from medications or diseases like leukemia, lymphoma, HIV/AIDS, pregnancy, untreated active tuberculosis, patients receiving stem cell transplant or antitumor necrosis factor agents (eg, adalimumab, infliximab, etanercept)/*Moderate or severe acute illness with or without fever, active herpes zoster infection, postherpetic neuropathy, concurrent drug therapy with antiviral medications, patients younger than 60 years of age
Adverse Effects	Local injection site reactions, flu-like symptoms, fever, diarrhea, headache
Drug Interactions	Acyclovir, valacyclovir, famciclovir, and immune globulins may diminish therapeutic effect of vaccine; immunosuppressants may enhance toxic effect of vaccine; PPSV may diminish vaccine effect; tuberculin test results may be diminished by live vaccine.
Monitoring	Fever, rash
Case Notes	Patients who want to protect themselves against herpes zoster infections (shingles) or those who want less-severe reactions to the disease should receive the herpes zoster vaccine. Herpes zoster is a preventable condition in individuals 60 years of age and older who have previously been exposed to the varicella-zoster virus (VZV). Administration of the vaccine can protect against development of herpes zoster, with the highest rate of efficacy in those aged 60-69. It may also reduce the severity of complications such as postherpetic neuralgia in patients who develop zoster following vaccination. The vaccine has to be stored frozen at 5°F or colder; the diluents can be stored at room temperature. Transmission to those susceptible to varicella infection from those who received the vaccine is rare unless a rash develops, then standard contact precautions should be exercised. Dosing for this vaccine is 0.65 cc SC into upper arm one time only. Separate the administration of the herpes zoster vaccine and the pneumococcal vaccine or other live vaccines by at least 4 weeks.

A 67-year-old patient presents to your pharmacy clinic for smoking cessation education. He is ready to quit in the next 30 days and would like assistance in setting a quit date as well as with the possible weight gain that is associated with smoking cessation. He has a past medical history of HTN, diabetes, dyslipidemia, and depression. He received his seasonal influenza vaccine 31 days ago with no report of adverse events. He received his most recent pneumococcal vaccination at the age of 61.

Allergies: NKDA

Medications: Lisinopril/hydrochlorothiazide 20/25 mg tablet 1 po daily; metformin 1,000 mg tablet 1 po twice daily; simvastatin 40 mg tablet 1 po at bedtime; fluoxetine 20 mg capsule 1 po daily; aspirin 81 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 215 lb Ht 73 in T 98.2°F BP 122/78 HR 64 RR 15

What additional vaccine does this patient need?

Pneumococcal Polysaccharide Vaccine 23-Valent (PPSV)	Inactivated pneumococcal vaccination (PPSV, pneumococcal conjugated vaccine [PCV])
Mechanism of Action	Antigens modulate an immune response, activating antibody production, which attacks, destroys, and eliminates the antigen, thus producing immunity through memory cells.
***Contraindications*/ Precautions**	*Severe allergic reaction to a previous vaccine dose or to a vaccine component*/Moderate or severe acute illness
Adverse Effects	Injection site reactions (eg, pain, swelling, redness), fever, myalgias
Drug Interactions	PPSV may be given with any other inactivated or live vaccine, with the exception of the herpes zoster vaccine due to decreased efficacy of zoster vaccine; PPSV and antibody-containing products may be given simultaneously at different sites or at any interval between doses; immunosuppressants may diminish the therapeutic effect of inactivated vaccines.
Monitoring	Monitor for syncope for at least 15 minutes following vaccination
Case Notes	Due to this patient's age, history of smoking, diabetes, and heart disease, and his most recent pneumococcal vaccination, he is due for his second dose. The vaccine protects against approximately 85% of serotypes known to cause invasive disease. This vaccine is recommended for all individuals 65 years of age and older, and those younger than 65 with chronic illnesses and conditions (eg, diabetes, pulmonary disease, cardiovascular disease, smoking, immunocompromised patients, those with HIV, chronic alcoholism, asplenia, chronic liver disease, kidney failure, and those with ESRD). Patients who require a dose of the vaccine before the age of 65 must receive an additional dose after 65. If a patient is less than five years from turning 65 at time of first dose, the patient must wait five years before receiving a second dose. After this second dose of PPSV, this patient will not require another PPSV dose in his lifetime. The dose of PPSV is 0.5 cc injected IM or SC. The PCV is recommended in children as a four-shot series, with those shots at months two, four, and six, and between 12 and 15 months.

The mother of an 8-year-old girl is picking up a refill from the pharmacy for her daughter. She says her daughter's appetite has decreased and is concerned that she might be losing weight. She has noticed the decrease in appetite over the past couple of months. Her daughter has a past medical history that is significant for attention deficit hyperactivity disorder (ADHD), perennial allergies, and obsessive compulsive disorder (OCD). ADHD and OCD were diagnosed four months ago.

Allergies: NKDA

Medications: Mometasone nasal spray 1 spray in each nostril once daily; paroxetine 20 mg tablet 1 po once daily; methylphenidate extended release 27 mg tablet 1 po once daily

Physical Exam/Other Studies:

Not available

Which one of her medications is most likely causing her decreased appetite?

Methylphenidate	Central nervous system stimulant (dexmethylphenidate, dextroamphetamine, lisdexamfetamine, methylphenidate)
Mechanism of Action	Blocks the reuptake of norepinephrine and dopamine into presynaptic neurons
***Contraindications*/ Precautions**	*Hypersensitivity, glaucoma, motor tics, Tourette's syndrome, use with or within 14 days following MAO inhibitor therapy, structural cardiac abnormalities, cardiomyopathy, coronary artery disease/*Heart failure, recent MI, hypertension, hyperthyroidism, seizures, emotional instability
Adverse Effects	Tachycardia, hypertension, arrhythmias, nervousness, insomnia, aggression, drowsiness, movement disorders, headache, weight loss, anorexia, nausea, thrombocytopenia, leukopenia, anemia, elevated LFTs
Drug Interactions	Avoid use with inhalational anesthetics & MAO inhibitors. May increase effects of clonidine, phenytoin, sympathomimetics, tricyclic antidepressants. May decrease effect of antihypertensives.
Monitoring	Evaluate for cardiac disease prior to initiation, CBC, blood pressure, heart rate, height, weight, appetite
Case Notes	Decreased appetite and weight loss are common side effects of stimulant therapy, and methylphenidate would be the most likely cause of this patient's symptoms. She should be referred to her physician for evaluation of growth. Although all stimulants can cause anorexia, this effect may be decreased by using a product with a shorter duration of action. Although food may affect the absorption of some dosage forms, many times it is necessary to take with food to minimize adverse effects and ensure adequate calorie intake.

A 15-year-old girl presents to her pediatrician's office to discuss therapy for ADHD. She was diagnosed with ADHD two months ago, and she and her family have been discussing treatment options. Her ADHD is characterized by hyperactivity and difficulty concentrating on tasks. Her past medical history is significant for depression with a history of suicidal thoughts. Her depression has responded well to medication and counseling. Her social history is significant for experimenting with marijuana and alcohol.

Allergies: NKDA

Medications: Fluoxetine 20 mg capsule 1 po once daily

Physical Exam/Other Studies:

Wt 124 lb Ht 62 in BP 105/71

Physical exam reveals no significant findings.

She and her family request a nonstimulant option for treatment of her ADHD. What medication would you recommend?

Guanfacine	Alpha$_2$-adrenergic agonist (clonidine, guanfacine)
Mechanism of Action	Stimulates alpha$_{2A}$-adrenoreceptors in the brain stem, thus regulating subcortical activity in the prefrontal cortex and decreasing sympathetic outflow
***Contraindications*/Precautions**	*Hypersensitivity*/Renal impairment, hepatic impairment, hypotension, heart block, bradycardia, syncope, coronary insufficiency, cerebrovascular disease
Adverse Effects	Bradycardia, hypotension, orthostatic hypotension, CNS depression, fatigue, abdominal pain, constipation, dry mouth
Drug Interactions	Alcohol and other CNS depressants; avoid giving with amifostine, major substrate of CYP3A4. Guanfacine is a CYP3A4 inhibitor.
Monitoring	Heart rate, blood pressure
Case Notes	Nonstimulant options for the treatment of ADHD include alpha$_2$-agonists, atomoxetine, bupropion, tricyclic antidepressants, and antipsychotics. Due to her history of suicidal thoughts and a drug interaction with fluoxetine, atomoxetine would not be recommended. Antipsychotics are typically reserved for resistant ADHD with comorbidities. Guanfacine and clonidine have each been used for ADHD. More rigorous clinical trials have been performed with guanfacine, its receptor selectivity decreases the risk for sedation, and it has a longer half-life compared with clonidine. The alpha$_2$-agonists are not as effective as stimulants in the treatment of ADHD but may decrease symptoms of hyperactivity, impulsiveness, and distractibility. To discontinue the medication, doses should be titrated slowly to avoid rebound hypertension and nervousness.

A 13-year-old boy presents to the behavioral clinic for follow-up. After completion and evaluation of the Vanderbilt Assessment Scales, the physician has diagnosed him with ADHD. His ADHD is characterized by impulsivity and inattention with very little hyperactivity. His past medical history is significant for Tourette's disorder. He was tried on methylphenidate in the past, which worsened his tics.

Allergies: NKDA

Medications: Clonidine 0.1 mg tablet 1 po three times daily; melatonin 3 mg tablet 1 po at bedtime

Physical Exam/Other Studies:

Wt 98 lb Ht 59 in T 98.7°F BP 100/68 HR 92

Physical exam reveals no significant findings.

What medication for ADHD might be recommended that will have a low risk for exacerbating this patient's tic disorder?

Atomoxetine	Selective norepinephrine reuptake inhibitor
Mechanism of Action	Selectively inhibits norepinephrine reuptake, enhancing norepinephrine activity
***Contraindications*/Precautions**	*Hypersensitivity, use with or within 14 days of MAO inhibitors, narrow-angle glaucoma*/Hypertension or other cardiovascular disease, cerebrovascular disease, Raynaud's phenomenon, urinary retention or bladder outlet obstruction, hepatic dysfunction, CYP2D6 poor metabolizers, bipolar disorder
Adverse Effects	Anorexia, weight loss, insomnia, depression, suicidal thinking, hypertension, orthostatic hypotension, syncope, headache, mood swings, irritability, aggression, nausea, liver injury, urinary retention
Drug Interactions	Major substrate of CYP2D6. May increase effects of $beta_2$-agonists, CNS depressants, and sympathomimetics
Monitoring	Evaluate for cardiac disease prior to starting. Weight, height, blood pressure, heart rate
Case Notes	Atomoxetine has not been linked to worsening tics. Methylphenidate or other stimulants may be used in combination with clonidine in patients with Tourette's disorder, but this patient's history of worsening when placed on methylphenidate would warrant finding an alternative. The starting dose of atomoxetine in patients <70 kg is 0.5 mg/kg/day, increasing after at least three days to 1.2 mg/kg/day. The dose may be titrated up to 1.4 mg/kg/day, not to exceed 100 mg/day. Doses may be given in the morning or divided into two doses, morning and afternoon. Based on the available dosage forms, this patient would start on 25 mg once daily. In patients who are receiving strong CYP2D6 inhibitors or who are poor metabolizers, the initial dose is maintained for four weeks and only increased if clinically needed and tolerated.

A 12-year-old girl presents to the physician to begin treatment for ADHD and depression. She was diagnosed with both after an extensive psychiatric evaluation two weeks ago. As part of her depression, she has not been eating well, which has caused weight loss. Her performance in school has greatly decreased compared to previous years. She has no other diagnosed medical conditions. Her father has a history of bipolar disorder, and her mother has Type 2 diabetes.

Allergies: NKDA

Medications: No medications

Physical Exam/Other Studies:

Wt 72 lb Ht 56 in BP 104/61 HR 94

Physical exam reveals no significant findings.

What antidepressant could be used in this patient that also has data for efficacy in treating ADHD?

Bupropion	Aminoketone antidepressant, dopamine reuptake inhibitor (no similar agents)
Mechanism of Action	Inhibits reuptake of norepinephrine and dopamine
***Contraindications*/ Precautions**	*Hypersensitivity, seizure disorder, anorexia/bulimia, use of MAO inhibitors within 14 days*/Cardiovascular disease, hypertension, hepatic or renal dysfunction
Adverse Effects	Tachycardia, hypertension, headache, insomnia, seizures, suicidal thoughts, decreased libido, weight loss, xerostomia, nausea, dyspepsia, serum sickness
Drug Interactions	Substrate of CYP2B6. Avoid use with MAO inhibitors.
Monitoring	Heart rate, blood pressure, weight
Case Notes	Bupropion is considered a second-line agent for the treatment of ADHD in children and adolescents. To decrease the number of medications that this child will receive, bupropion is an appropriate medication choice to treat both depression and ADHD. Tricyclic antidepressants also have some efficacy in ADHD, but would not be preferred due to adverse effects. All antidepressants carry a black box warning for increased risk of suicide in children and adolescents, and close monitoring is recommended during dose initiation and titration. The recommended starting dose of bupropion in children <15 years of age is 50 mg sustained release twice daily, titrated up to 300 mg/day in two divided doses. Bupropion is also a good choice for treatment of depression in those who are trying to quit smoking. Because bupropion does not have any serotonergic effects, it is a unique antidepressant.

A 23-year-old woman presents to her primary care physician due to what she thinks was a panic attack. She states that two days ago she had just finished taking an exam when she became dizzy, nauseated, and short of breath. She also states she was sweating and was very worried that she had failed the exam. This is the second time this has happened to her in the past two months. She reports that she is the type of person that is always worrying and feels anxious about something every day and is in constant fear that something bad is going to happen to her. She has no other medical conditions. Her mother has generalized anxiety disorder and hypertension. Her father is in good health.

Allergies: NKDA

Medications: Multivitamin tablet 1 po once daily

Physical Exam/Other Studies:

Physical exam reveals no significant findings.

The physician has diagnosed her with generalized anxiety disorder and will be starting her on an antidepressant. What other type of medication would be beneficial for her acute episodes of anxiety?

Benzodiazepine	Alprazolam, chlordiazepoxide, clonazepam, clorazepate, diazepam, lorazepam, oxazepam, triazolam, temazepam
Mechanism of Action	Interact with the $GABA_A$-receptor complex to enhance transmission of GABA, which is an inhibitory neurotransmitter
***Contraindications*/Precautions**	*Hypersensitivity, narrow-angle glaucoma, liver disease (clonazepam)*/Hepatic or renal disease
Adverse Effects	CNS depression, amnesia, poor memory, confusion, dependence, excess salivation
Drug Interactions	With the exception of lorazepam, all are major substrates of CYP3A4. Diazepam is also a major substrate of 2C19.
Monitoring	CNS depression, respiratory rate. LFT and CBC with long-term use.
Case Notes	Antidepressants are the drugs of choice for treating generalized anxiety disorder; however, benzodiazepines are used for short-term relief for acute symptoms and while the antidepressant is reaching its therapeutic effect. Benzodiazepines are effective in the majority of patients. Dependence is expected with long-term use, so doses should be slowly titrated to discontinue and they should be avoided in patients with chemical dependency. All benzodiazepines are expected to be effective when given in equivalent doses. Lorazepam and oxazepam are preferred for patients with reduced hepatic function. Oxazepam has the shortest half-life. Oxazepam and lorazepam take longer to achieve peak concentrations (two to four hours) compared to the other agents.

A 62-year-old man presents to his physician's office complaining of feeling restless. For the past three days, he has noticed that he cannot sit still and has begun pacing and tapping his feet uncontrollably. His past medical history is significant for bipolar disorder and hypertension. One week ago, he was diagnosed with prostatitis and started on ciprofloxacin.

Allergies: Cephalexin (hives)

Medications: Haloperidol 5 mg tablet 1 po every eight hours; lamotrigine 100 mg tablet 1 po twice daily; lisinopril 10 mg tablet 1 po once daily; ciprofloxacin 500 mg tablet 1 po twice daily for 28 days

Physical Exam/Other Studies:

Wt 184 lb Ht 73 in BP 132/84 HR 78

Physical exam reveals that he is tapping his toes and moving his legs nonstop. Otherwise, no significant findings on exam.

Which one of his medications is likely causing his symptoms?

Haloperidol	First-generation antipsychotic (chlorpromazine, fluphenazine, haloperidol, loxapine, mesoridazine, molindone, perphenazine, pimozide, thioridazine, trifluoperazine, thiothixene)
Mechanism of Action	Competitively blocks postsynaptic dopamine receptors. Also blocks alpha-adrenergic and cholinergic activity.
***Contraindications*/ Precautions**	*Hypersensitivity, narrow-angle glaucoma, bone marrow suppression, severe liver or cardiac disease, parkinsonism*/QT prolongation, renal or hepatic dysfunction, cardiovascular disease, seizures, angina
Adverse Effects	Tachycardia, hypertension, ECG changes, extrapyramidal reactions, drowsiness, euphoria, depression, hyperglycemia, gynecomastia, anticholinergic effects
Drug Interactions	Major substrate of CYP2D6 and 3A4. Inhibits CYP2D6 and 3A4.
Monitoring	Blood pressure, heart rate, CBC, LFTs, ECG, extrapyramidal symptoms
Case Notes	This patient is presenting with akathisia, likely due to a drug interaction between ciprofloxacin and haloperidol. Akathisia is an extrapyramidal reaction that is more common with first-generation antipsychotics than second-generation antipsychotics. In this patient, either reducing the dose of haloperidol or changing the antibiotic could be helpful in reducing the symptoms. Beta-blockers such as propranolol, nadolol, or metoprolol, as well as benzodiazepines, have been used in the treatment of extrapyramidal reactions to antipsychotics. If the akathisia persists, he would benefit from changing to a second-generation antipsychotic, with quetiapine and clozapine having the lowest risk for akathisia.

A 45-year-old man presents to the pharmacy to pick up his prescription refills. He asks the pharmacist if any of his medications would cause him to be more thirsty and to urinate more than usual. He has noticed these symptoms for the past two weeks, and they seem to be worsening. His past medical history is significant for bipolar disorder and hypertension. Both are presently well controlled. His social history is negative for alcohol or illicit drug intake as well as tobacco use.

Allergies: NKDA

Medications: Valproic acid 500 mg tablet 2 po twice daily; propranolol 120 mg tablet 1 po once daily; lithium 450 mg tablet 2 po twice daily

Physical Exam/Other Studies:

Not available

Which of his medications has the potential to cause polyuria and polydipsia?

Lithium	Mood stabilizer, antimanic
Mechanism of Action	Alters ion transport across cell membranes and possibly increases reuptake of serotonin and norepinephrine
***Contraindications*/ Precautions**	*Hypersensitivity/*Cardiovascular disease, thyroid disease, use with medications that alter sodium excretion, significant fluid loss, renal dysfunction
Adverse Effects	Gastrointestinal upset, diarrhea, tremor (50% of patients), polyuria and polydipsia (70% of patients), diabetes insipidus, glomerular sclerosis, hypothyroidism, poor concentration, alopecia, weight gain, metallic taste, acute lithium toxicity
Drug Interactions	Many exist; consult drug interaction resource for detailed information. Avoid use with sibutramine. Thiazide diuretics, nonsteroidal anti-inflammatory drugs, and angiotensin-converting enzyme inhibitors may significantly increase the risk for life-threatening lithium toxicity.
Monitoring	CBC, chemistry, lipids, renal function, thyroid function, and serum lithium concentration at baseline, weekly until stabilized, and then every 6-12 months
Case Notes	Lithium is a first-line agent for maintenance therapy of bipolar disorder, especially for symptoms of mania. Lithium is superior to other mood-stabilizing drugs in reducing suicide risk. Lithium inhibits vasopressin, thus decreasing the kidney's ability to concentrate urine, resulting in increased urine volume and frequency. This adverse effect may be present in up to 70% of patients treated with lithium. If urine loss exceeds 3 L/day, then the patient has diabetes insipidus. Hyperglycemia should be ruled out as a cause of polyuria and polydipsia. The dosage of lithium is titrated to a concentration of 0.6-1.4 mEq/L. Levels over 2 mEq/L place the patient at risk for acute lithium toxicity, which can be life-threatening. Other mood-stabilizing medications include valproic acid, carbamazepine, lamotrigine, and oxcarbazepine.

A 38-year-old man was brought to the hospital two days ago by the police. He had an episode at the public library where he was disruptive and accusing everyone in the library of conspiring to kill him. He became very combative and was treated initially with haloperidol intramuscularly. He has since been evaluated and diagnosed with schizophrenia. Illnesses that may present with these symptoms have been ruled out. His past medical history is unknown as he claims that he was abducted and given medications that erased his memory. His family has been found and is returning from a trip and will arrive at the hospital soon.

Allergies: NKDA

Medications: Haloperidol 2 mg intramuscularly every four hours as needed

Physical Exam/Other Studies:

Wt 205 lb Ht 72 in BP 121/74 HR 82

Physical exam reveals no significant findings.

He needs to be started on an oral medication for his schizophrenia. Which of the following medications would generally be considered a first-line treatment for schizophrenia?

A. clozapine
B. haloperidol
C. quetiapine
D. venlafaxine

Quetiapine	Second-generation or atypical antipsychotic (aripiprazole, asenapine, clozapine, iloperidone, olanzapine, paliperidone, quetiapine, risperidone, ziprasidone)
Mechanism of Action	Dopamine type 2 and serotonin type 2 receptor antagonism are responsible for antipsychotic activity. Also an antagonist at serotonin type 1A, dopamine type 1, histamine type 1, alpha type 1, and alpha type 2 receptors.
***Contraindications*/ Precautions**	Dementia, suicidal thinking, arrhythmias, patients at risk for aspiration pneumonia, diabetes, hyperlipidemia, orthostatic hypotension, hepatic impairment, Parkinson's disease, renal impairment, seizures, thyroid disease
Adverse Effects	Elevated blood pressure, somnolence, headache, fatigue, extrapyramidal symptoms, dyslipidemia, hyperglycemia, weight gain, elevated prolactin, nausea, suicidal thinking, anticholinergic effects, cardiac conduction alteration, cataracts
Drug Interactions	Major substrate of CYP3A4
Monitoring	Lipid profile, blood glucose/HbA1c, weight, ophthalmic exam every six months
Case Notes	Recommended initial therapy for schizophrenia is with a second-generation antipsychotic. While first-generation antipsychotics, such as haloperidol, are effective, the risk for extrapyramidal adverse effects is higher. Disadvantages of second-generation antipsychotics include the risk for metabolic and cardiovascular effects as well as increased cost compared to the first-generation agents. Risperidone and paliperidone are available in long-acting formulations for those who are not adherent to therapy. As each product may have different drug interactions and toxicities, please refer to the individual agent monographs for more complete information. Clozapine is effective but may cause life-threatening blood dyscrasias, and thus is reserved for resistant cases or in those with frequent suicide attempts. Venlafaxine is not expected to provide benefit for schizophrenia.

A 28-year-old woman presents to her physician for treatment of depression. She has had symptoms of depressed mood for about six months and has been sleeping most of the day when not working. She has not had any thoughts of suicide. Her past medical history is significant for migraines. Her social history is significant for one to two alcoholic beverages daily.

Allergies: NKDA

Medications: Propranolol LA 160 mg tablet 1 po once daily; sumatriptan 50 mg tablet 1 po PRN migraine

Physical Exam/Other Studies:

Wt 128 lb Ht 65 in BP 118/72 HR 68

Physical exam reveals no significant findings.

What type of antidepressant could be used for this patient to help with both migraines and depression?

Tricyclic Antidepressant	Tertiary amines (amitriptyline, clomipramine, doxepin, imipramine); secondary amines (desipramine, nortriptyline)
Mechanism of Action	Inhibit norepinephrine and serotonin reuptake
***Contraindications*/ Precautions**	*Hypersensitivity, narrow-angle glaucoma, use of MAO inhibitors within 14 days, use during recovery from MI*/Cardiovascular disease, seizures, diabetes, urinary retention, bowel obstruction, hepatic or renal dysfunction, hyperthyroidism, thyroid replacement therapy, orthostatic hypotension
Adverse Effects	Anticholinergic effects, orthostatic hypotension, arrhythmias, sedation, seizures, suicidal thinking, weight gain, disorders of glucose metabolism, cholestatic jaundice
Drug Interactions	Substrate of CYP2D6. Avoid use with MAO inhibitors, sibutramine, thioridazine, and ziprasidone. Multiple interactions exist.
Monitoring	Heart rate, blood pressure, weight
Case Notes	Tricyclic antidepressants (TCA) are recommended for patients with both depression and migraines. Propranolol would need to be weaned slowly as the TCA is titrated. The TCAs vary in their norepinephrine (NE) and serotonin (5-HT) effects with secondary amines having more effect on NE and tertiary amines having greater effect on 5-HT. Anticholinergic effects, sedation, orthostatic hypotension, seizures, and cardiac conduction abnormalities are greater with tertiary amines, making secondary amines typically better tolerated. Patients should be closely monitored for suicidal thoughts as overdose with TCAs is life-threatening. When discontinuing, doses should be tapered slowly to avoid withdrawal symptoms.

A 32-year-old man presents to the pharmacy to check his blood pressure. He tells you that the machine read his blood pressure at 174/93 and when he took it again, after resting for five minutes, it was 170/92. He states that he started new medications for depression and anxiety one week ago and his physician told him to check his blood pressure every three days. Prior to starting the medicine, his blood pressure had been well controlled on an antihypertensive and was 125/72 in his physician's office and 132/81 when he checked it three days ago.

Allergies: Lisinopril (angioedema)

Medications: Hydrochlorothiazide 25 mg tablet 1 po once daily; venlafaxine XR 75 mg capsule 1 po once a day; clonazepam 0.5 mg tablet ½ tablet po twice daily

Physical Exam/Other Studies:
BP 170/92 HR 74

Which of his medications may be causing his elevated blood pressure?

Venlafaxine	Serotonin and norepinephrine reuptake inhibitor antidepressant (duloxetine, venlafaxine)
Mechanism of Action	Inhibit serotonin and norepinephrine reuptake
***Contraindications*/ Precautions**	*Hypersensitivity, use of MAO inhibitor within 14 days*/Hypertension, renal impairment, hepatic impairment, seizures, unstable cardiac disease, diuretic therapy or volume depletion, narrow-angle glaucoma, abnormal platelet function
Adverse Effects	Hypertension, headache, insomnia, yawning, anorexia, weight loss, SIADH, nausea, altered taste, sexual dysfunction, abnormal bleeding, mydriasis
Drug Interactions	Many potential drug interactions exist. Avoid use with MAO inhibitors and sibutramine. Substrate of CYP2D6 and 3A4. Weak inhibitor of CYP2B6, 2D6, and 3A4.
Monitoring	Blood pressure, renal and hepatic function, weight, cholesterol, sodium, mental status, suicidal ideation
Case Notes	Venlafaxine is associated with elevated blood pressure, especially in those with underlying hypertension. Patients should be counseled to check their blood pressure periodically when starting venlafaxine and with any increase in dose. Venlafaxine should be given with food. The contents of the capsule may be sprinkled on applesauce and swallowed. Anyone who has received venlafaxine for greater than one week should taper the dose to avoid withdrawal symptoms. Those receiving therapy for more than six weeks should taper over two weeks. Duloxetine is generally used for the treatment of neuropathic pain. This patient should be referred to his physician to report this adverse effect and consider changing to a different antidepressant.

A 26-year-old woman presents to the physician for follow-up on depression. While her mood and concentration are improved, she continues to complain of insomnia. She was diagnosed with major depressive disorder six months ago and has been trying different antidepressants. Initially, she was started on paroxetine, followed by citalopram and nefazodone. She tried each agent at the maximum dose for eight weeks. Each helped with her depression but did not alleviate her insomnia. Varying the time of day of antidepressant administration has not been helpful. She has tried over-the-counter melatonin, which has not helped her insomnia. She has no other past medical history.

Allergies: NKDA

Medications: Nefazodone 250 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 172 lb Ht 63 in T 98.5°F BP 121/78

Physical exam reveals no significant findings.

The physician would like to change her therapy to something that might better control her insomnia. What antidepressant would you recommend?

Mirtazapine	Alpha$_2$-antagonist antidepressant, tetracyclic antidepressant
Mechanism of Action	Central presynaptic alpha$_2$-adrenergic antagonist. Also acts as a serotonin, histamine, alpha$_1$-adrenergic, and muscarinic receptor antagonist.
***Contraindications*/ Precautions**	*Hypersensitivity, use of MAO inhibitor within 14 days*/Decreased GI motility, urinary retention, BPH, hyperlipidemia, orthostatic hypotension, hepatic impairment, renal impairment, seizure disorder, elderly
Adverse Effects	Somnolence, increased cholesterol, anticholinergic effects (constipation, dry mouth), increased appetite, weight gain, dizziness, weakness, orthostatic hypotension, agranulocytosis (rarely)
Drug Interactions	Multiple drug interactions exist. Avoid use with MAO inhibitors and sibutramine. Mirtazapine is a strong CYP1A2, 2D6, and 3A4 substrate.
Monitoring	CBC, lipid profile, mental status, suicide ideation
Case Notes	Mirtazapine is the most sedating of the antidepressants due to its effects on adrenergic and histamine receptors and would be a reasonable choice in this patient. The starting dose is 15 mg at night, increasing every one to two weeks up to 45 mg/day. Her nefazodone should be tapered off while titrating the mirtazapine. Geriatric patients require lower starting doses. Mirtazapine has the potential for physiological dependence, abuse, and/or tolerance. Mirtazapine has a low incidence of sexual dysfunction and may be useful for patients with this comorbidity or who have experienced sexual dysfunction as an adverse effect of other antidepressants. Many clinicians may choose to add an agent to assist with insomnia rather than changing therapy, especially if the patient has had a positive response to the antidepressant.

A 52-year-old man presents to his physician to discuss concerns with his sexual function. He reports that he is having difficulty attaining and maintaining an erection. He noticed these symptoms about a month ago and feels that it has worsened over the last two weeks. His past medical history is significant for major depressive disorder and seizure disorder. He was previously treated with mirtazapine for depression, which caused excess sedation. His current antidepressant was started about two months ago. His depression and seizures are well controlled on his current therapy.

Allergies: Carbamazepine (rash)

Medications: Sertraline 100 mg tablet 1 po once daily; topiramate 100 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 234 lb Ht 72 in BP 130/81

Physical exam reveals no significant findings.

What antidepressant is associated with a low risk for sexual dysfunction and would be appropriate to switch to in this patient?

Nefazodone	Serotonin reuptake inhibitor and antagonist (nefazodone, trazodone)
Mechanism of Action	Inhibits reuptake of serotonin and norepinephrine and blocks 5-HT_2 and $alpha_1$ receptors
***Contraindications*/Precautions**	*Hypersensitivity, use with carbamazepine, astemizole, pimozide, or triazolam, active liver disease, elevated LFT*/Seizures, orthostatic hypotension, unstable heart disease.
Adverse Effects	Orthostatic hypotension, headache, drowsiness, liver failure, GI upset, taste perversion, urinary retention, abnormal vision, elevated blood pressure
Drug Interactions	Many drug interactions exist. Do not use with alprazolam, carbamazepine, cisapride, eplerenone, everolimus, nisoldipine, pimozide, ranolazine, salmeterol, sibutramine, tolvaptan, or triazolam. Nefazodone is a substrate of CYP2D6 and 3A4 and an inhibitor of CYP3A4.
Monitoring	Blood pressure, liver enzymes, mental status, suicidal ideation
Case Notes	Bupropion, mirtazapine, and nefazodone are antidepressants with the lowest risk for causing sexual dysfunction. Bupropion is contraindicated due to his seizure disorder, and mirtazapine was not tolerated in the past. Seizures have been reported with nefazodone, but the risk would be lower than with bupropion. The usual starting dose is 100 mg twice daily, increased every one to two weeks up to 600 mg/day in two divided doses. His sertraline dose will need to be tapered while starting nefazodone. Patients should be counseled to report any yellowing of the skin or eyes, lack of appetite for several days, dark urine, severe nausea, abdominal pain, or weakness as these may be signs of liver disease.

A 12-year-old girl presents to her pediatrician after being diagnosed with major depressive disorder by a psychiatrist. The pediatrician will be starting her on a medication at today's visit. She has no other past medical history. Family history is significant for depression in both mother and father.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 100 lb Ht 60 in BP 102/62 HR 75

Physical exam reveals no significant findings.

This patient needs to be started on an antidepressant. Which antidepressant is recommended first-line for the treatment of depression in children and adolescents?

Fluoxetine	Selective serotonin reuptake inhibitor (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline, St John's wort)
Mechanism of Action	Inhibits reuptake of serotonin in the CNS
***Contraindications*/ Precautions**	*Hypersensitivity, use of MAO inhibitor within 14 days, use with thioridazine or pimozide*/Impaired platelet aggregation, use with medications that impair platelet aggregation, anorexia, renal or hepatic impairment, seizure disorder, third trimester of pregnancy, use with diuretics, suicidal risk
Adverse Effects	Headache, insomnia, somnolence, anxiety, irritability, suicidal thinking, hyperactivity, sexual dysfunction, weight loss, nausea, dyspepsia, altered platelet function (rare)
Drug Interactions	Many drug interactions exist. Fluoxetine is a major substrate of CYP2C9, 2D6, and 3A4 and a strong inhibitor of 2D6 and moderate inhibitor of 1A2 and 2C19. Other SSRIs have fewer drug interactions; consult individual drug monographs for drug interaction information.
Monitoring	Weight, mental status, suicidal thoughts
Case Notes	To date, fluoxetine is the only antidepressant with adequate evidence of efficacy in children and adolescents and is therefore recommended as first-line therapy. Other antidepressants may be used if comorbidities warrant their use or if fluoxetine is not effective or tolerated. Of all of the selective serotonin reuptake inhibitors (SSRIs), fluoxetine has the longest half-life and highest number of drug interactions. It is more likely to cause insomnia and should not be given after 4 PM Adverse effects of all SSRIs are similar, but some patients may respond more favorably to a different agent in the same class. Children and adolescents have a higher risk for behavioral disturbances and insomnia while being treated with SSRIs compared to adults. As with all antidepressants, patients treated with SSRIs should be closely monitored for suicidal thinking.

A 35-year-old woman presents to the pharmacy counter complaining of trouble falling asleep. She came in approximately one week ago and you noted that she has very poor sleep hygiene. She sleeps with the television on, reads and works in bed, sleeps short hours during the week and long hours on the weekend, and takes naps when she gets home from work. You advised her to continue her current medications and try getting on a more normal sleep schedule. She has done these things and still is unable to get sleep. She has had no success with diphenhydramine (50 mg at bedtime) or melatonin (5 mg at bedtime) and has stopped both of these therapies. She is hoping you have a recommendation on what she should do next.

Allergies: NKDA

Medications: Trazodone 100 mg tablet 1 po at bedtime; multivitamin tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 140 lb Ht 64 in T 98.6°F BP 120/78 HR 70

What is the best pharmacologic recommendation for this patient to help her sleep?

Benzodiazepine Receptor Antagonist	Estazolam, eszopiclone, flurazepam, quazepam, temazepam, triazolam, zaleplon, zolpidem
Mechanism of Action	Selectively binds to the $GABA_A$ receptors and effectively induces sleepiness; increases stage 2 sleep and decreases REM and delta sleep
***Contraindications*/ Precautions**	*Hypersensitivity*/Abnormal thinking, behavioral changes, CNS depression, hypersensitivity reactions, sleep-related activities, depression, drug abuse, hepatic impairment, myasthenia gravis, respiratory disease
Adverse Effects	Adverse effects are dose related. Common effects are drowsiness, amnesia, dizziness, headache, GI effects, and rare effects of weight gain due to sleep-eating and psychotic reactions.
Drug Interactions	Major substrates of CYP3A4; may increase levels of ethyl alcohol, CNS depressants, methotrimeprazine
Monitoring	Daytime alertness, respiratory rate, behavior profile
Case Notes	A benzodiazepine receptor antagonist like zolpidem, zaleplon, or eszopiclone is a good choice for this patient. Zolpidem comes in an immediate-release, sublingual, and an extended-release tablet, and all are to be taken immediately before bedtime. Elderly patients and those with hepatic impairment require dose adjustments. Zolpidem will help reduce sleep latency and nocturnal awakenings, increasing total sleep time. Zaleplon helps most at decreasing number of middle-of-the-night awakenings. Treatment with these medications should be limited; seek specific limits from individual drug monographs. This will minimize tolerance and dependence. Increasing trazodone is an option, but 100 mg is the maximum recommended dose for this indication. Increasing the dose of diphenhydramine will not increase the response. Melatonin is commonly used for sleep, but its use is not well-supported by clinical studies.

A 54-year-old man presents to your clinic for a check-up. He has a past medical history of chronic alcoholism, hypertension, dyslipidemia, and restless leg syndrome. He does not smoke but drinks approximately a half-liter of whiskey every night. He has discussed with you the need to quit drinking, but was not ready at previous visits. He does not consider himself an alcoholic, but does know that something needs to change.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po every morning; simvastatin 10 mg tablet 1 po every evening

Physical Exam/Other Studies:

Wt 210 lb Ht 67 in T 98.8°F BP 148/98 HR 102 RR 18

Physical exam reveals ataxia and nystagmus.

Na 135 K 3.5 Cl 102 fasting glucose 102 SCr 1.2 AST 240 ALT 98 AST/ALT 2.4

After discussing with this patient his LFT results as well as his AST/ALT ratio that indicates he has alcoholic liver disease, he realizes he needs help quitting alcohol and asks if there is any medication that can help make the transition easier.

What medication exhibits its action by causing an adverse reaction when combined with alcohol?

Disulfiram	Aldehyde dehydrogenase inhibitor
Mechanism of Action	Disulfiram is a thiuram derivative that inhibits the metabolism of aldehyde dehydrogenase. When taken with alcohol, acetaldehyde levels in the body increase, causing adverse reactions of severe nausea and flushing.
***Contraindications*/ Precautions**	*Hypersensitivity, patients receiving ethanol, metronidazole, paraldehyde, or ethanol-containing preparations like cough syrup or tonics; psychosis; severe myocardial disease and coronary occlusion*/Hepatotoxicity, diabetes, hypothyroidism, nephritis, seizures, ethanol intoxication
Adverse Effects	When taken with alcohol, one can expect flushing, nausea, thirst, palpitations, chest pain, vertigo, and hypotension. Other adverse effects include rash, metallic aftertaste, impotence, peripheral neuritis, optic neuritis, and hepatitis.
Drug Interactions	Strong inhibitor of CYP2E1; avoid use with alcohol, amprenavir, ritonavir, sertraline; avoid cough syrups and elixirs with alcohol, vinegars, cider, extracts, and foods containing ethanol.
Monitoring	Hypokalemia, LFT at baseline and after 10-14 days, CBC, serum chemistries
Case Notes	Disulfiram helps deter patients from drinking by causing uncomfortable side effects when it is combined with alcohol. It should not be administered to the patient until he or she has abstained from alcohol for at least 12 hours. Initial oral dose is 500 mg daily for one to two weeks. Maintenance dose is 250 mg daily for months to years, depending on when the patient is fully recovered. This medication, although still available, has fallen out of favor to newer medicines like naltrexone and acamprosate, both of which reduce the cravings for alcohol. Other medications, such as ceftriaxone, griseofulvin, metronidazole, and procarbazine, can cause a disulfiram-like reaction to alcohol.

A 33-year-old woman is brought to the emergency department by an ambulance and is suffering from signs of drug intoxication. She was found on the street near a bar. She is unable to provide an account of what happened to her or why she is in the state that she is. She has severe slurred speech, slow reaction times, and is unable to walk on her own. Emergency medical personnel found an empty bottle of oxycodone in her purse, as well as a bottle of alprazolam and a bottle of what smells like ethyl alcohol.

Allergies: Unknown

Medications: Alprazolam 2 mg tablet 1 po three times daily as needed (there are 28 pills remaining in a prescription of 30 filled one day ago); oxycodone 10 mg tablet 1 po three times daily as needed (there are no pills remaining in a bottle of 90 filled approximately seven days ago); other medications unknown at this time

Physical Exam/Other Studies:

Wt 128 lb Ht 66 in T 98.1°F BP 142/92 HR 98 RR 14 O_2 sat 99%

Physical exam reveals mydriasis, piloerection, depressed respiration.

Labs are drawn upon admission; results unavailable.

She is admitted to the hospital to be treated for drug intoxication. Upon admission, she goes unconscious and is unable to be woken.

What medication should be used to treat this patient's acute opiate intoxication?

Naloxone	Opioid antagonist (nalmefene, naltrexone, naloxone)
Mechanism of Action	Pure opioid antagonist that competes and displaces narcotics at opioid receptor sites
***Contraindications*/ Precautions**	*Hypersensitivity*/Acute opioid withdrawal if patient is dependent; cardiovascular disease; seizures
Adverse Effects	CNS withdrawal symptoms
Drug Interactions	No significant drug interactions exist.
Monitoring	RR, HR, BP, temperature, level of consciousness, ABGs or pulse oximetry
Case Notes	Opioid antagonists, and naloxone specifically, are the drugs of choice for treatment of opiate intoxication. Her signs, symptoms, physical exam characteristics, and the empty bottle of oxycodone lead you to believe this is the condition from which she is suffering. Naloxone should be dosed 0.4-2 mg IV every three minutes until she responds to this treatment. If she does not respond after 10 mg of naloxone administered, she most likely is suffering from an overdose of a different substance. At this point, you should consider other causes of respiratory depression. Toxicology will guide treatment in this situation. These medications are also helpful in diagnosing opioid dependence. Because the action of naloxone is rapid, the symptoms of opiate overdose may persist, such as respiratory depression. Patients should be observed very closely and monitored for this effect.

A 34-year-old woman presents to your diabetes clinic for a follow-up visit. She reports no complaints with her Type 2 diabetes today. She was diagnosed approximately two years ago and was started on oral therapy. She is tolerating the therapy well, but is becoming more concerned about her general health. Approximately three months ago, her mother died of a heart attack at age 64, and the doctors said that it was most likely because she was diabetic. She is concerned that she will meet a similar fate. Her past medical history consists of obesity, hypertension, sleep apnea, dyslipidemia, and Type 2 diabetes. She smokes approximately one pack/day for 10 years, but is ready to quit. She says she needs help quitting, as her "cold turkey" attempts have never been successful. She has no prescription insurance coverage at this time.

Allergies: NKDA

Medications: Glipizide 10 mg tablet 1 po twice daily; metformin 1,000 mg tablet 1 po twice daily; lisinopril 20 mg tablet 1 po daily; pravastatin 20 mg tablet 1 po every evening

Physical Exam/Other Studies:

Wt 260 lb Ht 68 in BP 148/86 HR 70 RR 18

Foot exam reveals no loss of sensation in feet per monofilament exam, (+) bilateral pedal pulses, (+) onychomycosis.

Na 137 K 4.0 Cl 100 A1c 8.7% fasting glucose 145 SCr 1.0

TC 278 HDL 39 LDL 138 TG 239 Non-HDL 177

After discussing with this patient her results from testing, she becomes even more concerned with her health. She asks you what you believe she should do to help improve her chances of avoiding a heart attack. Along with eating healthily, exercising regularly, weight loss, and medication adherence, you recommend she quit smoking. You discuss that smoking is putting her at even higher risk of having a coronary event. She agrees it is time to quit and asks for a suggestion on what to take since she has never taken anything before.

What is the best recommendation for this patient to help her quit smoking?

Nicotine	Nicotine replacement therapy (gum, patch, lozenge, nasal spray, inhaler)
Mechanism of Action	Stimulates CNS at nicotine-specific receptors, reducing physical withdrawal symptoms
***Contraindications*/ Precautions**	*Hypersensitivity, a patient smoking during postmyocardial infarction period, a life-threatening arrhythmia, severe angina pectoris, TMJ disease (gum), pregnancy, nonsmoker*/Cardiovascular disease (weigh risk vs. benefit, close monitoring necessary), insulin-dependent diabetes, GI disease, hepatic or renal impairment, hyperthyroidism, individual dosage form specific precautions (see individual monographs)
Adverse Effects	Side effects are dependent on dosage form used. Symptoms of nicotine toxicity include headache, nausea and vomiting, abdominal pain, diarrhea, salivation, dizziness, blurred vision, weakness, cold sweat, mental confusion, weakness, and in severe overdose, hypotension, seizures, and respiratory depression.
Drug Interactions	Increases levels of adenosine, nicotine levels increased by cimetidine; decreases levels of peginterferon alfa-2b; acidic food/beverages decrease absorption of nicotine from gum
Monitoring	HR, BP, signs of toxicity, discontinue if a rash develops with patch
Case Notes	A patient who has never tried pharmacotherapy to quit smoking should stick with a first-line treatment, and because this patient has no prescription insurance, NRT is the most affordable choice for her. The nicotine gum, lozenge, and patch can be purchased without a prescription. The nicotine nasal spray and inhaler require a prescription. The patch and gum are available as generics. To avoid NRT-related side effects, she should stop smoking when using any of these products. Most products are dosed based on number of cigarettes smoked per day. If used during pregnancy, choose a product with intermittent dosing. If a patch is selected, remove overnight due to insomnia. Smoking cessation may improve patients with dyslipidemia in addition to decreasing risk of heart disease.

A 45-year-old man presents to the pharmacy clinic to follow up on a previous smoking cessation visit. The patient was started on bupropion approximately one month ago and has been experiencing symptoms of nervousness and tremors, and will sometimes convulse, according to his wife. He started convulsing approximately one week ago and has had two episodes total. Since beginning the bupropion, he has been able to refrain from smoking cigarettes, but has had a total of seven days where he has slipped and smoked approximately three cigarettes each of those days. His history of smoking cessation includes unsuccessful attempts at using nicotine replacement therapies (patch, gum, and lozenge). He has a history of HTN, dyslipidemia, nicotine addiction, and occasional GERD.

Allergies: NKDA

Medications: Bupropion 150 mg tablet 1 po twice daily; hydrochlorothiazide 25 mg tablet 1 po daily; rosuvastatin 20 mg tablet 1 po daily; ranitidine 150 mg tablet 1 po twice daily as needed

Physical Exam/Other Studies:

Wt 179 lb Ht 69 in T 98.7°F BP 146/87 HR 88 RR 18

Based on his recent seizure episodes, his bupropion should be discontinued. He should begin another smoking cessation therapy to help him abstain from smoking.

What is the best medication for smoking cessation for this patient?

Varenicline	Partial nicotine agonist
Mechanism of Action	Partial neuronal alpha$_4$-beta$_2$-nicotinic receptor agonist; prevents nicotine stimulation of mesolimbic dopamine system associated with nicotine addiction. Also stimulates dopamine activity but to a much smaller degree than nicotine does, resulting in decreased cravings and withdrawal symptoms.
***Contraindications/* Precautions**	*Hypersensitivity*/Neuropsychiatric events (depression, suicidal thoughts, suicide), dose-dependent nausea, hypersensitivity reactions (angioedema, Stevens-Johnson syndrome), sedation, psychiatric illness, renal impairment
Adverse Effects	Insomnia, headache, abnormal dreams, dose-related nausea, sleep disorders, somnolence, nightmares, lethargy, malaise, rash, GI symptoms, upper respiratory tract disorder, dyspnea
Drug Interactions	Safety and efficacy of varenicline with other smoking cessation therapies have not been established. No significant drug interactions exist.
Monitoring	Behavioral changes and psychiatric symptoms
Case Notes	Varenicline is a good option in a patient who cannot tolerate other smoking cessation therapies. Because this patient has had adverse reactions to bupropion and was unsuccessful with his attempt with nicotine replacement therapies, varenicline should be started. This medication is typically initiated one week prior to the patient's quit date, but is still appropriate for this patient who has already quit. Initial adult dosing is for days one through three, 0.5 mg once daily, then days four through seven, 0.5 mg twice daily. Maintenance dosing is 1 mg twice daily for day eight through week 12. If the patient successfully quits in 12 weeks, the patient may choose to continue another 12 weeks to maintain success. If the patient is unsuccessful at quitting in 12 weeks of therapy, discontinue and reassess for reasons of failure. Administer with food and a glass of water to prevent GI symptoms. A dose reduction may be warranted if symptoms are intolerable.

A 48-year-old man presents to the nephrology clinic for a follow-up visit. His past medical history includes chronic kidney disease secondary to diabetes mellitus Type 1 and hypertension.

Allergies: NKDA

Medications: Insulin aspart injection 10 units subcutaneously with meals; insulin glargine injection 25 units subcutaneously at bedtime; lisinopril 20 mg tablet 1 po once daily; amlodipine 10 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 172 lb Ht 69 in T 98.7°F BP 128/75 HR 72 RR 16 O_2 sat 98%

Physical exam is unremarkable.

Ca 8.4 PO_4 9.8 Alb 2.4 SCr 4.5

In addition to dietary phosphorus restriction, what medication could be started to treat his high level of phosphate?

A. calcium carbonate
B. calcium acetate
C. aluminum hydroxide
D. sevelamer

Sevelamer	Phosphate binder (calcium carbonate, calcium acetate, aluminum hydroxide, sevelamer, lanthanum carbonate)
Mechanism of Action	Binds phosphate within the intestinal lumen, limiting absorption and decreasing serum phosphate concentrations without altering calcium, aluminum, or bicarbonate concentrations (sevelamar only)
***Contraindications*/ Precautions**	*Hypophosphatemia*/Use with caution in patients with gastrointestinal disease
Adverse Effects	Pruritus, vomiting, nausea, diarrhea, dyspepsia, limb pain, arthralgia, nasopharyngitis, bronchitis
Drug Interactions	Sevelamer may decrease the serum concentrations of levothyroxine, mycophenolate, and quinolone antibiotics.
Monitoring	Serum chemistry
Case Notes	There are several agents that are used in the treatment of hyperphosphatemia in patients with kidney disease. Typically, treatment is initiated with calcium-containing agents unless the serum calcium concentration is above 10.2 mg/dL or the calcium-phosphate product is greater than 55, like it is in this patient. Aluminum-containing agents are not used due to concerns about aluminum toxicity. Since sevelamer does not contain calcium, it does not cause hypercalcemia and would be a good choice in this patient. Patients should be instructed to take tablets or capsules whole. The usual initial dose is 800-1,600 mg daily divided and given with meals. Lanthanum carbonate could also be used in this situation since it does not contain calcium. It is not absorbed and has a high affinity for phosphorus. Often, combinations of calcium and non–calcium-containing phosphate binders may be necessary in patients with hyperphosphatemia and hypocalcemia.

A 48-year-old man presents to the nephrology clinic for an initial visit. He was sent by his primary care physician after he complained of fatigue and weakness. His laboratory work showed a significant anemia. His past medical history includes chronic kidney disease secondary to diabetes mellitus Type 1 and hypertension.

Allergies: NKDA

Medications: Insulin aspart injection 10 units subcutaneously with meals; insulin glargine injection 25 units subcutaneously at bedtime; lisinopril 20 mg tablet 1 po once daily; amlodipine 10 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 172 lb Ht 69 in T 98.7°F BP 128/75 HR 72 RR 16 O_2 sat 98%

Physical exam is unremarkable.

Hg 8.2 HCT 25 Plt 152 SCr 4.5

Iron studies were conducted and were all within the appropriate range.

What should be used to treat his anemia?

Erythropoiesis Stimulating Agent	Epoetin alfa, darbepoetin alfa
Mechanism of Action	Induces erythropoiesis by stimulating the division and differentiation of committed erythroid progenitor cells; induces the release of reticulocytes from the bone marrow into the bloodstream, where they mature to erythrocytes. This results in an increase in reticulocyte counts followed by a rise in hematocrit and hemoglobin levels.
***Contraindications*/ Precautions**	*Hypersensitivity to the agent or any component of the formulation, uncontrolled hypertension/*Cancer patients, cardiovascular events, chronic renal failure patients, allergic reactions, pure red cell aplasia; use with caution in patients with hematologic disease, hypertension, cardiovascular disease, perisurgical patients, seizures, severe anemia, acute bleeding
Adverse Effects	Hypertension, thrombotic events, fever, dizziness, insomnia, headache, pruritus, nausea, vomiting, diarrhea
Drug Interactions	No significant interactions exist.
Monitoring	Blood pressure, CBC, iron studies, serum chemistry
Case Notes	Erythropoiesis stimulating agents are indicated for the treatment of anemia in patients with chronic kidney disease once iron stores have been determined to be adequate. They are also used in many other types of anemia. Due to increased concerns about thromboembolic events and decreased survival in certain patient populations, the reader should refer to the package information for updated information. For use in patients with chronic kidney disease, the target hemoglobin concentration is between 11-12 g/dL and not more than 13 g/dL. These agents are given either intravenously or subcutaneously at a dose individualized for each patient. For patients with kidney disease, typically 50-100 units/kg three times weekly of epoetin alfa or 0.45 mcg/kg once weekly for darbepoetin alfa is used.

A 38-year-old woman presents to the nephrology clinic for a routine follow-up exam. Her past medical history is significant for IgA nephropathy for which she has been on hemodialysis three times weekly for the past five years.

Allergies: NKDA

Medications: Calcium carbonate 500 mg tablet (OTC) 1 po three times daily with meals; epoetin alfa injection 5,000 units intravenously twice weekly; iron sucrose injection 100 mg intravenously three times weekly; paricalcitol injection 1 mcg intravenously three times weekly; renal multivitamin tablet 1 po once daily

Physical Exam/Other Studies:

Not available

A medical student on her first day in the clinic asks you which of the patient's medications is being used to control the parathyroid hormone and prevent renal osteodystrophy. What is your answer?

Paricalcitol	Vitamin D analog (paricalcitol and doxercalciferol)
Mechanism of Action	Reduces parathyroid hormone levels and improves calcium and phosphate homeostasis by binding to and activating the vitamin D receptor in the kidney, parathyroid gland, intestine, and bone.
***Contraindications*/ Precautions**	*Hypersensitivity to paricalcitol, vitamin D toxicity, hypercalcemia*/May result in excessive vitamin D and hypercalcemia
Adverse Effects	Nausea, diarrhea, infection
Drug Interactions	Substrate of CYP3A4; bile acid sequestrants and orlistat may decrease serum concentrations of paricalcitol; paricalcitol may enhance digoxin toxicity
Monitoring	Signs/symptoms of vitamin D toxicity, calcium, phosphate, serum or plasma intact parathyroid hormone
Case Notes	The vitamin D compounds ergocalciferol and cholecalciferol have to be converted to the active form in the kidney. Calcitriol is the most active form of vitamin D, while the vitamin D analogs are paricalcitol and doxercalciferol. Patients who have severe (stage 5) chronic kidney disease require either calcitriol or one of the vitamin D analogs since they do not require the kidney for conversion to the active form. These agents are used in chronic kidney disease to prevent renal osteodystrophy. The recommendations for specific vitamin D therapy vary depending on stage of kidney disease, 25-hydroxyvitamin D levels, and parathyroid hormone levels. Prior to initiating therapy, phosphorus and calcium levels should be well controlled to minimize the risk of hypercalcemia. For patients who have elevated calcium levels, the calcimimetic cinacalcet may be used instead of or in conjunction with the vitamin D analogs.

A 73-year-old man presents for his usual hemodialysis appointment complaining of severe muscle weakness. He has a past medical history of hypertension and end-stage kidney disease on hemodialysis for the past three months.

Allergies: NKDA

Medications: Aspirin 81 mg tablet (OTC) 1 po once daily; amlodipine 10 mg tablet 1 po once daily; enalapril 10 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 192 lb Ht 68 in T 97.5°F BP 124/70 HR 72 RR 16 O_2 sat 98%

Physical exam reveals no significant findings.

K 7.8 CO_2 16 BUN 45 SCr 8.1 Glu 98

ECG reveals an increased PR interval and a widened QRS complex.

He is diagnosed with hyperkalemia and treated with calcium gluconate, insulin with dextrose, albuterol nebulization, and sodium bicarbonate along with his normal hemodialysis.

What medication could be used between hemodialysis sessions to prevent hyperkalemia in this patient?

Sodium Polystyrene Sulfonate (SPS)	Ion-exchange resin
Mechanism of Action	Removes potassium by exchanging sodium ions for potassium ions in the intestine
***Contraindications*/ Precautions**	*Hypersensitivity to sodium polystyrene sulfonate, any component of the formulation, obstructive bowel disease, oral administration in neonates; concerns in using with sorbitol: rectal administration in neonates or use in any postoperative patient until normal bowel function resumes*/Colonic necrosis, electrolyte disturbances, fecal impaction, hypokalemia; use with caution in cardiovascular disease, edema, renal impairment, the elderly, and pediatrics
Adverse Effects	Hypernatremia, hypokalemia, hypomagnesemia, sodium retention, anorexia, diarrhea, constipation, nausea, vomiting
Drug Interactions	SPS may enhance the toxicities of aluminium hydroxide and digoxin; antacids, laxatives, and sorbitol may enhance the toxicities of SPS; SPS may decrease the serum concentration of lithium.
Monitoring	Serum electrolytes and ECG
Case Notes	Hemodialysis would be the most effective way to remove potassium for this patient. However, it is not uncommon for dialysis patients to become hyperkalemic between their routinely scheduled dialysis sessions. SPS is one way to remove potassium from the body. Each gram of SPS exchanges 1 mEq of sodium for 1 mEq of potassium. SPS can be administered orally or rectally, and the onset of action is one to two hours after administration. This patient should probably also have his ACE inhibitor changed to an antihypertensive agent that does not cause hyperkalemia.

A 46-year-old woman presents to your pharmacy counter to pick up a prescription for ciprofloxacin 250 mg tablets to treat a urinary tract infection. Her past medical history is significant for hypertension, diabetes mellitus Type 2, and gastroesophageal reflux disease.

Allergies: Sulfa (rash)

Medications: Calcium carbonate 500 mg tablets (OTC) 1 po three times daily; famotidine 20 mg tablets 1 po twice daily; hydrochlorothiazide 25 mg tablet 1 po once daily; lisinopril 20 mg tablet 1 po once daily; metformin 500 mg tablets 1 po twice daily

Physical Exam/Other Studies:
Not available

Which of her medications may interact with the ciprofloxacin, resulting in decreased efficacy of the antimicrobial agent?

Calcium Carbonate	Calcium salt (calcium acetate, calcium carbonate, calcium chloride, calcium citrate, calcium glubionate, calcium gluconate, calcium lactate, calcium phosphate)
Mechanism of Action	Used as a dietary supplement to prevent or treat calcium imbalance. Used as an antacid to neutralize gastric acidity resulting in increased gastric and duodenal pH.
***Contraindications*/ Precautions**	*Hypercalcemia, renal calculi, hypophosphatemia, patients with suspected digoxin toxicity*/ Gastrointestinal effects, achlorhydria, hypoparathyroid disease, kidney stones
Adverse Effects	Headache, hypophosphatemia, hypercalcemia, constipation, laxative effect, acid rebound, nausea, vomiting, anorexia, milk-alkali syndrome with high or chronic dosing
Drug Interactions	Calcium salts may bind to many medications and render them inactive (such as the fluoroquinolones). Many other drug interactions exist. Refer to product information for specific interactions.
Monitoring	Calcium, phosphate, renal function; ECG, vital signs, and watch for extravasation with IV use
Case Notes	Calcium salts may decrease the absorption of quinolone or tetracycline antibiotics and should be administered separately from these agents. Calcium in its many salt forms can be used in a variety of disease states. In addition to use for hypocalcemia, calcium may be used as phosphate binder in kidney disease, as an antacid, and for the prevention of osteoporosis. Calcium is best absorbed if taken with food (some salts do not require this) and with vitamin D. Adults should intake between 1,000-1,200 mg of calcium per day in divided doses. The dose of calcium depends on the indication for use but is typically expressed in terms of elemental calcium. Each calcium product may contain a different amount of elemental calcium per tablet or capsule, so care should be used to determine the correct dose for each patient.

A 26-year-old man is admitted to the intensive care unit with a diagnosis of diabetic ketoacidosis. His past medical history is significant for diabetes mellitus Type 1. He is treated according to the hospital's diabetic ketoacidosis protocol.

Allergies: NKDA

Medications: Insulin drip titrated per the hospital's protocol

Physical Exam/Other Studies:

Wt 142 lb Ht 66 in T 98.7°F BP 120/70 HR 82 RR 16 O_2 sat 98%

Physical exam is unremarkable.

Na 128 K 3.6 Cl 111 CO_2 16 BUN 27 SCr 2.07 Glu 276 PO_4 0.9

The above labs were drawn six hours after initiation of the insulin drip.

What medication should be used to treat the hypophosphatemia?

Potassium Phosphate	Phosphate replacement (potassium phosphate, sodium phosphate)
Mechanism of Action	Replaces phosphate
***Contraindications/* Precautions**	*Hypersensitivity to the agent or any component of the formulation, hyperphosphatemia, hyperkalemia, hypocalcemia, hypomagnesemia, renal failure/*Use with caution in acid/base disorders, cardiovascular disease, potassium-altering conditions or disorders, renal impairment, digitalis, parenteral administration
Adverse Effects	Confusion, weakness, hyperkalemia, diarrhea, nausea, vomiting
Drug Interactions	Use with caution with medications that increase potassium; calcium salts, antacids, iron salts, magnesium salts, and sucralfate may decrease the absorption of phosphate supplementation.
Monitoring	Serum electrolytes and cardiac monitoring (especially when giving parenterally)
Case Notes	Phosphate replacement may be given either orally or intravenously using either potassium phosphate or sodium phosphate. In diabetic ketoacidosis, it is common for the phosphate to decrease during treatment with insulin. In this patient's case, the phosphate level is <1, which is considered severe enough to warrant intravenous therapy. Since the potassium is on the low end of normal, potassium phosphate would be an acceptable choice for treatment. A wide range of dosing recommendations is available, and the dose depends on the degree of hypophosphatemia. For intravenous treatment, doses range from 0.08-0.64 mmol/kg. There are multiple oral products available, and due to similar names, they are often confused. The oral dose is 1.5-2 g/day in divided doses. The dose-limiting side effect of oral treatment is diarrhea.

A 46-year-old man presents for a follow-up visit with his primary care physician. Six months ago, he was diagnosed with hypertension. He tried lifestyle modifications for several months, but he was unsuccessful in lowering his blood pressure. Three months ago, he was initiated on an antihypertensive, and this visit is a follow-up to monitor blood pressure and laboratory findings.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 182 lb Ht 69 in T 98.7°F BP 138/85 HR 72 RR 16 O_2 sat 98%

Physical exam is unremarkable.

Na 134 K 3.6 Cl 109 BUN 12 SCr 0.7 Mg 1.2

What should be used to treat his hypomagnesemia?

Magnesium Supplementation	Magnesium oxide, magnesium sulfate, magnesium-containing antacids, magnesium chloride, magnesium lactate
Mechanism of Action	Replaces magnesium
***Contraindications*/ Precautions**	*Hypersensitivity to any component of the formulation*/Use with caution in self-treatment of constipation, neuromuscular disease, renal impairment
Adverse Effects	Diarrhea
Drug Interactions	Magnesium salts may decrease the absorption of bisphosphonates, quinolone antibiotics, and tetracycline antibiotics; magnesium salts may enhance the effects of neuromuscular blockers; calcitriol may increase the serum concentration of magnesium salts; calcium channel blockers may enhance the adverse effects of magnesium salts; magnesium salts may enhance the adverse effects of calcium and sodium polystyrene sulfonate; magnesium salts may decrease the serum concentrations of eltrombopag, trientine, mycophenolate, and phosphate supplements; trientine may decrease the serum concentration of magnesium salts.
Monitoring	Serum electrolytes and cardiac monitoring (especially when giving parenterally)
Case Notes	Magnesium replacement may be given either intravenously or orally depending on the degree of hypomagnesemia and symptoms present. This patient is likely experiencing decreased levels of potassium and magnesium due to his hydrochlorothiazide therapy. Treatment with an oral product, such as magnesium oxide 400 mg three times daily, would be beneficial for this patient. Magnesium sulfate given via continuous infusion or as an intramuscular injection is also used to prevent seizures in pregnant women with pre-eclampsia. It is also the treatment for torsade de pointes and may be used in the treatment of acute exacerbations of asthma.

A 31-year-old woman presents to the emergency department complaining of malaise, weakness, and leg cramps for the past two days. She has been experiencing multiple episodes of vomiting and diarrhea and has not been able to eat or drink like usual.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 132 lb Ht 63 in T 99.1°F BP 118/68 HR 82 RR 16 O_2 sat 98%

Physical exam reveals poor skin turgor and dry mucous membranes

Na 137 K 2.9 Cl 100 CO_2 33 BUN 30 SCr 1.2 Glu 78

ECG reveals T wave inversions.

She is diagnosed with gastroenteritis and hypokalemia secondary to her vomiting and diarrhea.

What medication should be used to treat the hypokalemia?

Potassium Supplementation	Potassium chloride, potassium phosphate, potassium bicarbonate, potassium acetate, potassium citrate, potassium gluconate
Mechanism of Action	Replaces potassium, the major intracellular cation
***Contraindications*/ Precautions**	*Hypersensitivity to the agent or any component of the formulation, hyperkalemia, the solid/oral dosage form should not be used in any patient with a delay or arrest in gastrointestinal motility*/Use with caution in acid/base disorders, cardiovascular disease, potassium-altering conditions or disorders, renal impairment, digitalis, parenteral administration
Adverse Effects	Rash, hyperkalemia, abdominal pain or discomfort, diarrhea, nausea, vomiting
Drug Interactions	Use with caution with medications that increase potassium; anticholinergic agents may enhance the ulcerogenic effect of potassium supplements
Monitoring	Serum electrolytes and cardiac monitoring (especially when giving parenterally)
Case Notes	Potassium chloride is the most common agent used to treat hypokalemia. It can be given either orally or parenterally, but the oral route is the preferred route of administration. The parenteral route should be used in patients who cannot tolerate oral supplementation or in patients with severe or symptomatic hypokalemia. Normally, potassium chloride is infused at a rate of 10 mEq/hour, but in situations of careful cardiac monitoring, it may be infused more quickly. Potassium must always be diluted prior to parenteral administration. Typically 10-20 mEq can be diluted in 100 mL of 0.9% sodium chloride for peripheral administration. When situations require quick administration and under cardiac monitoring, 40-60 mEq may be diluted in 1,000 mL of 0.9% sodium chloride. Depending on the degree of hypokalemia, doses of 40-120 mEq of potassium may be needed. The oral dose should be divided into three or four doses to help diminish the gastrointestinal effects.

A 54-year-old woman presents to the emergency department complaining of abdominal pain. She was recently hospitalized for three days following a laparoscopic cholecystectomy. In the emergency department, she is noted to be hypotensive and tachycardic.

Allergies: Amoxicillin (anaphylaxis)

Medications: No home medications

Physical Exam/Other Studies:

Wt 272 lb Ht 64 in T 97.5°F BP 85/55 HR 112 RR 24 O_2 sat 78%

Physical exam reveals no significant findings.

SCr 1.48 WBC 14.1 Lactic acid 5.1 INR 1.45

The emergency room physician is concerned that the patient may have sepsis.

What therapy should be used initially to help restore her blood pressure?

Normal Saline	Intravenous fluids (dextrose 5% in water, 0.45% sodium chloride, 0.9% sodium chloride, 3% sodium chloride, lactated ringers, and many others)
Mechanism of Action	Helps to restore fluid and electrolyte balance, osmotic pressure, and water distribution
***Contraindications*/ Precautions**	*Hypersensitivity to sodium chloride, any component of the formulation, hypertonic uterus, hypernatremia, fluid retention/*Hyponatremia, sodium toxicity, use with caution in cirrhosis, edema, heart failure, hypertension, renal impairment
Adverse Effects	Heart failure, extravasation, hypervolemia, hypernatremia, hypokalemia, pulmonary edema, and rarely: central pontine myelinolysis due to rapid correction of hyponatremia
Drug Interactions	Sodium chloride may increase the excretion of lithium; sodium chloride may enhance the adverse or toxic effects of tolvaptan.
Monitoring	Serum sodium, potassium, chloride, bicarbonate, intake and output, weight
Case Notes	Volume resuscitation in sepsis is best accomplished with the use of intravenous fluids, specifically normal saline. This will help to replenish extracellular volume and improve tissue perfusion. Isotonic fluids, like normal saline or lactated ringers, are best for treating hypovolemia. Other intravenous fluids are used to correct electrolyte disorders, or to provide maintenance therapy in patients who cannot eat or drink. The choice of fluids used in these situations is highly dependent on patient electrolyte levels (sodium and potassium primarily), and degree of ongoing losses. Hypertonic fluids such as 3% sodium chloride should be restricted to use only in severe, symptomatic hyponatremia and under the close supervision of a physician. When treating disorders of sodium homeostasis, it is important to correct the problem slowly, as too rapid of a correction can lead to detrimental adverse effects.

A 13-year-old boy presents to your pharmacy with his mother and she states he is complaining of runny nose, itchy and watery eyes, and nasal congestion. It has been going on for one month without relief. He is having trouble focusing in school because of his symptoms. He has no past medical history. He lives at home with his mom, dad, and two brothers (ages 4 years and 6 months). His mother reports he is exposed to tobacco in the home because dad smokes approximately half of a pack/day. The family has two pets (one dog and one cat). He says he enjoys playing soccer but lately has not felt well enough to participate.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Wt 68 lb Ht 52 in T 97.6°F

Physical exam reveals positive Dennie's lines, no purulent nasal discharge.

This patient is suffering from nasal congestion and allergic rhinitis symptoms. When asked, his mother tells you he does know how to swallow tablets and would prefer this to a nasal spray.

In addition to an oral decongestant for his congestion, what medication would you recommend for this patient?

Loratadine	Antihistamine (nonselective: brompheniramine, chlorpheniramine, dexchlorpheniramine, carbinoxamine, clemastine, diphenhydramine, pyrilamine, tripelennamine, promethazine, cyproheptadine, phenindamine, azelastine; selective: loratadine, desloratadine, fexofenadine, cetirizine, levocetirizine)
Mechanism of Action	Blocks H_1-receptors preventing mediator release; may also decrease cellular recruitment
***Contraindications*/ Precautions**	*Hypersensitivity to loratadine or any component of the formulation*/Hepatic impairment, renal impairment, pediatrics less than 2 years of age; phenylalanine is contained in some formulations
Adverse Effects	Headache, sedation (at higher doses), fatigue, xerostomia, possible CNS stimulation in children
Drug Interactions	Moderate substrate of the CYP2C19 isoenzyme; loratadine may increase the level of alcohol, anticholinergics, CNS depressants; levels of loratadine may be increased by P-glycoprotein inhibitors, pramlintide; loratadine may decrease the levels of acetylcholinesterase inhibitors, betahistine; levels of loratadine may be decreased by acetylcholinesterase inhibitors, amphetamines, peginterferon alfa-2b, P-glycoprotein inducers
Monitoring	Allergic rhinitis symptoms
Case Notes	Loratadine is the best choice for this patient because it is a nonsedating antihistamine. He should be advised to take this medication on an empty stomach, as food may delay the peak of the drug. Patients age 6 and older should take 10 mg po daily, and pediatrics ages 2 through 5 should take 5 mg po daily. A liquid formulation is available for this medication. Nonselective antihistamines will most likely be a cheaper alternative, but caution should be taken when recommending them because of their side effects of drowsiness, dizziness, and somnolence. Nonpharmacologic recommendations should also be made for this patient (eg, limit smoke exposure in home, removal of pet dander). Diphenhydramine, a sedating antihistamine, is an FDA-approved sleep aid.

A 29-year-old pregnant woman presents to your pharmacy one week after picking up her regular prescription refills of cetirizine and birth control. She tells you that she has just taken four pregnancy tests, all of which have come back as positive. She believes she conceived approximately five weeks ago. She has stopped her birth control pills, but wants your advice on if she should stop her cetirizine as well. She has an appointment to see her OB/GYN in three weeks, but wanted to speak with you because her allergies are really bothersome this time of year and she is concerned she will not have any relief if she stops her current antihistamine.

Allergies: NKDA

Medications: Cetirizine 10 mg tablet (OTC) 1 po daily; ethinyl estradiol/drospirenone 0.02 mg/3 mg tablet 1 po daily (stopped 1 week ago)

Physical Exam/Other Studies:

Wt 125 lb Ht 64 in BP 118/76 HR 64

You recommend this patient discontinue her medications and keep her current appointment with her OB/GYN. However, you do know that there is a medication that is safe in pregnancy to help her with her allergic rhinitis.

What is the best medication to treat this patient's allergic rhinitis during her pregnancy?

Cromolyn	Mast cell stabilizer
Mechanism of Action	Prevents the mast cell release of histamine, leukotrienes, and slow-reacting substance of anaphylaxis by inhibiting degranulation after contact with allergens
***Contraindications/* Precautions**	*Hypersensitivity to cromolyn or a component of its formulation, acute asthma attacks/* Anaphylaxis, cardiovascular disease (specifically cardiac arrhythmias)
Adverse Effects	Sneezing, burning, stinging, irritation, headache, unpleasant taste, hoarseness, cough, postnasal drip
Drug Interactions	There are no known significant drug interactions.
Monitoring	Allergy symptoms
Case Notes	Intranasal cromolyn is first line for allergic rhinitis in pregnant and lactating females. Cromolyn should be used as a prophylactic therapy only, as it takes approximately two to four weeks to see the full effect from therapy. It is not effective in rescue situations. If a patient with seasonal allergic rhinitis is interested in using cromolyn, it is recommended they begin the therapy approximately one month before the onset of allergy symptoms. Directions for use are to instill one spray in each nostril three to four times daily after clearing the nasal passages by using nasal saline spray or wash and/or blowing nose. It is available over-the-counter. Cromolyn is also available in inhaled, oral, and ophthalmic formulations. Inhaled cromolyn is used as an adjunct in allergic and asthma disorders as well as prevention of exercise-induced bronchospasm. The oral formulation is for use in systemic mastocytosis. Ophthalmic cromolyn is used to treat vernal keratoconjunctivitis, conjunctivitis, and keratitis.

A 10-year-old boy presents to the asthma clinic with his mother for evaluation. He also suffers from perennial allergic rhinitis. He was started on loratadine approximately three months ago but has not had much relief from this addition to his regimen. Currently, he complains of sneezing, rhinorrhea, itching eyes, and nasal congestion. He lives with his parents in the country and has two cats that live outside. He goes to public school, but is currently on summer break and is spending a lot of time outside playing with his siblings. He is up to date with all of his vaccines and got an influenza vaccine this last fall. His father suffers from seasonal allergic rhinitis, and mother has no diagnoses of relevance.

Allergies: NKDA

Medications: Fluticasone HFA inhaler 44 mcg 2 inhalations po twice daily; loratadine 10 mg tablet (OTC) 1 po every morning; acetaminophen 325 mg tablet (OTC) 1 po every six hours PRN headache

Physical Exam/Other Studies:

Wt 60 lb Ht 55 in T 98.6°F BP 110/78 HR 86 RR 16 O_2 sat 99%

Physical exam reveals allergic rhinitis signs of allergic shiners and gape.

PEF 280 (90% of personal best) FEV_1 85%

This patient has perennial allergic rhinitis that is not responding to his loratadine. Another agent should be added.

What class of medications should be added to adequately control his current allergic rhinitis symptoms?

Intranasal Corticosteroid	Beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone, triamcinolone
Mechanism of Action	Reduces inflammation by reducing mediator release, suppresses neutrophil chemotaxis, reduces intracellular edema, causes mild vasoconstriction, and inhibits mast cell-mediated late-phase reactions
***Contraindications/* Precautions**	*Hypersensitivity*/Adrenal suppression, bronchospasm, delayed wound healing, immunosuppression, Kaposi's sarcoma, psychiatric disturbances; refer to individual product labeling for more information on precautions
Adverse Effects	Sneezing, stinging, headache, cough, epistaxis, local *Candida albicans* infections, and possible growth suppression with higher bioavailability (eg, beclomethasone); nasal steroids have been found to have no significant association with hypothalamic-pituitary axis suppression, cataract formation, glaucoma, or bone mineral density changes
Drug Interactions	Avoid use with aldesleukin, BCG, natalizumab, live vaccines, and echinacea
Monitoring	Growth, signs and symptoms of HPA axis suppression/adrenal insufficiency, eosinophilic conditions
Case Notes	Because the patient is suffering from nasal symptoms of allergic rhinitis, a topical intranasal steroid is the best choice to add to his regimen. Review individual agents for dosing recommendations. Some patients may notice an improvement in symptoms in a few days, but with others, it may take two to three weeks to see a peak effect. Counsel patients on continued use until efficacy can be determined. To administer a nasal spray, prime the pump by spraying until a fine mist appears. Have the patient blow his or her nose or use a nasal saline spray or wash to clear out mucus before using the nasal corticosteroid. Shake well prior to use. Have patient tilt head slightly forward and keep bottle upright when administering sprays. Breathe in gently through the nostril, and then breathe out through the mouth.

A 40-year-old man presents to your pharmacy counter asking for something that will relieve his nasal congestion. He has been suffering with this congestion for about two days now. He has found no relief with nasal saline wash but has not tried anything orally. He suffers from hypertension and intermittent allergic rhinitis with congestion every fall.

Allergies: NKDA

Medications: Metoprolol succinate extended release 50 mg tablet 1 po twice daily; cetirizine 10 mg tablet (OTC) 1 po every evening; aspirin 81 mg tablet (OTC) 1 po daily; multivitamin tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 200 lb Ht 72 in BP 138/84 HR 72

Physical exam not performed.

What medication is the best choice for this patient to improve his congestion?

Oxymetazoline	Topical decongestant (phenylephrine, naphazoline, tetrahydrozoline, oxymetazoline, xylometazoline)
Mechanism of Action	Stimulates alpha-adrenergic receptors in the arterioles of the nasal mucosa to produce vasoconstriction
***Contraindications*/ Precautions**	*Hypersensitivity to oxymetazoline or any component of the formulation*/Rebound congestion, glaucoma
Adverse Effects	Hypertension, palpitation, transient burning, stinging, drying of the nasal mucosa, rebound congestion with prolonged use, sneezing
Drug Interactions	Avoid use with MAO inhibitors; increased toxicity may be observed when used with sympathomimetics, atomoxetine, cannabinoids, MAO inhibitors, tricyclic antidepressants
Monitoring	Resolution of nasal congestion, adverse effects
Case Notes	Oxymetazoline is the best choice for this patient due to the presence of hypertension. Systemic decongestants such as phenylephrine or pseudoephedrine carry the risk of raising the blood pressure; therefore, topical agents are preferred. Some systemic absorption may occur, but if used correctly, the side effects should be minimal. Patients should be instructed to instill two to three sprays in each nostril twice daily, not to exceed three days of continued use. Continued use for more than three days could result in rhinitis medicamentosa, or rebound congestion, which results in more severe nasal congestion that responds less to nasal decongestants. Ocular formulations of decongestants also exist and may be used to help decrease erythema of the eye.

A 70-year-old woman presents to your clinic complaining of shortness of breath and dyspnea on exertion. She has been a two pack/day smoker for the past 40 years and has no intentions on quitting despite numerous discussions. Her current medical conditions include chronic bronchitis, COPD, and hypertension. She lives in an assisted living facility. In the past, she has been resistant to therapies that require multiple administrations throughout the day. Therapies that are only dosed once daily are preferred.

Allergies: Morphine (hives)

Medications: Albuterol HFA inhaler 1-2 puffs every four to six hours PRN for shortness of breath; valsartan 80 mg tablet 1 po daily; multivitamin tablet (OTC) 1 po daily

Physical Exam/Other Studies:

Wt 140 lb Ht 65 in T 98.1°F BP 130/78 HR 70 RR 22 O_2 sat 98%

Physical exam reveals acutely worsening dyspnea, increased sputum volume, end-expiratory wheezes. Previous spirometry values one month ago are FEV_1/FVC 65%, FEV_1 85%. Because of acute exacerbation, patient defers spirometry today.

This patient is experiencing an acute exacerbation of her COPD. Previously, she was in stage I (mild) COPD with grade 0 dyspnea (not troubled by breathlessness except with strenuous exercise). Today, her classification is unavailable, but her dyspnea grade has increased to 3 (severe dyspnea–stops for breath after walking 100 yards or after a few minutes on a level surface).

What medication could be added to this patient's regimen to help control her COPD and sputum production?

Tiotropium	Anticholinergic (long-acting: tiotropium; short-acting: ipratropium, atropine)
Mechanism of Action	Competitively and reversibly inhibits the action of acetylcholine at muscarinic receptors in bronchial smooth muscle, blocking the cholinergic effects of bronchoconstriction and mucus secretion
Contraindications/ **Precautions**	*Hypersensitivity, lactose allergy*/Paradoxical bronchospasm, glaucoma, myasthenia gravis, prostatic hyperplasia, renal impairment
Adverse Effects	Xerostomia, upper respiratory tract infection, sinusitis, chest pain, edema, depression, dysphonia, rash, dyspepsia, constipation, vomiting, GERD, myalgias, pharyngitis, epistaxis, urinary retention, tachycardia, blurred vision, and symptoms of narrow-angle glaucoma
Drug Interactions	Tiotropium may increase the levels of anticholinergics, cannabinoids, potassium chloride; tiotropium levels may be increased by pramlintide; tiotropium may decrease the levels of anticholinesterase inhibitors, secretin; the levels of tiotropium may be decreased by anticholinesterase inhibitors, peginterferon alfa-2b
Monitoring	FEV_1, peak flow
Case Notes	Because of the antisecretory effects of anticholinergics and because it also helps as a bronchodilator, tiotropium is the best choice for this patient. It is dosed by inhaling the contents of one capsule (18 mcg) through a specific inhalation device once daily, which is most advantageous for this patient who prefers once-daily regimens. The capsule should not be taken orally. This medication is not to be used as a rescue medication, but as a long-term controller medication. It should be taken at the same time each day. Be sure to counsel the patient to follow the instructions carefully when administering this medication. Ipratropium dosed two puffs four times daily could also benefit this patient; however, it is dosed two inhalations four times daily. A combination of ipratropium plus albuterol also exists.

A 75-year-old man presents to your pharmacy to refill his medications. He smoked for 20 years (approximately one pack/day) and was diagnosed with COPD three years ago. After diagnosis, he quit smoking, although he reports that he recently started smoking again approximately one month ago. Currently he has stage III COPD, and today he presents with grade 1 dyspnea (troubled by shortness of breath when hurrying on a level surface or walking up a slight hill). Today he does not complain of increased sputum production or severe dyspnea on exertion. He also suffers from diabetes, dyslipidemia, hypertension, and epilepsy.

Allergies: Eggs (rash), meperidine (hives)

Medications: Glipizide 5 mg tablet 1 po twice daily; insulin aspart subcutaneous injection as directed by sliding scale; aspirin 81 mg tablet (OTC) 1 po daily; lisinopril 5 mg tablet 1 po daily; simvastatin 40 mg tablet 1 po every evening; furosemide 40 mg tablet 1 po every morning; citalopram 40 mg tablet 1 po at bedtime; hydrochlorothiazide 25 mg tablet 1 po every morning; fluticasone/salmeterol 500 mcg/50 mcg inhalation 1 puff po every morning and evening; ipratropium/albuterol 18 mcg/90 mcg inhalation 2 puffs po four times daily; theophylline CR 200 mg tablet 1 po every 12 hours; phenytoin 100 mg capsule 1 po three times daily

Physical Exam/Other Studies:

Wt 156 lb Ht 70 in BP 122/82 HR 80 RR 18 O_2 sat 99%

Physical exam reveals no pertinent findings.

What medication on this patient's profile should be discontinued due to its narrow therapeutic index and multiple drug interactions?

Theophylline	Methylxanthine (theophylline, aminophylline)
Mechanism of Action	Causes bronchodilation, diuresis, CNS and cardiac stimulation, and gastric acid secretion by blocking phosphodiesterase, which increases tissue concentrations of cyclic AMP, which in turn promotes catecholamine stimulation of lipolysis, glycogenolysis, and gluconeogenesis and induces release of epinephrine from adrenal medulla cells
***Contraindications*/ Precautions**	*Hypersensitivity, corn allergy*/Tachyarrhythmia, hyperthyroidism, peptic ulcer disease, seizure disorder
Adverse Effects	Dyspepsia, nausea, vomiting, diarrhea, headache, dizziness, tachycardia; arrhythmias and seizures indicate more severe toxicity. See product labeling for more complete list.
Drug Interactions	Major substrate of CYP1A2, 2E1, 3A4; decreased theophylline clearance when combined with cimetidine, macrolides, fluoroquinolones; enhanced theophylline clearance when combined with tobacco and marijuana smoking, phenytoin, phenobarbital, rifampin
Monitoring	Heart rate, CNS effects, respiratory rate, arterial blood gases, theophylline serum levels
Case Notes	Theophylline may have a place in COPD therapy in patients who have not received a good clinical response from inhaled beta-agonists and anticholinergics. However, this patient has recently started smoking, which increases theophylline clearance. Because of the narrow therapeutic window of this medication and its effects on the cardiovascular system, it is rarely recommended in clinical practice due to drug interaction and toxicity potential. Theophylline is dosed 200 mg twice daily titrated up to between 400 mg and 900 mg per day in divided doses. Peak theophylline levels should fall between 5-15 mcg/mL. Toxicity usually develops at levels over 20 mcg/mL. The IV form, aminophylline, is also available for use.

A 21-year-old woman presents to the pharmacy to ask for a recommendation for her nasal congestion. She has had a runny nose, nasal congestion, headache, and sore throat for three days. She has been using saline sinus rinses, a topical nasal decongestant, and an antihistamine for the past three days. While the topical nasal decongestant has been helpful, it only provides relief for about two hours. Her past medical history is significant for seasonal allergies.

Allergies: NKDA

Medications: Cetirizine 10 mg tablet (OTC) 1 po once daily; oxymetazoline 0.05% nasal spray (OTC) two sprays in each nostril twice a day

What type of systemic over-the-counter product would you recommend for this patient to help with her nasal congestion?

Alpha-Adrenergic Agonist Decongestant	Phenylephrine, pseudoephedrine
Mechanism of Action	Stimulates alpha-adrenergic receptors of the respiratory mucosa, causing vasoconstriction
***Contraindications*/ Precautions**	*Hypersensitivity, use with MAO inhibitor, uncontrolled hypertension, severe coronary artery disease/*Hyperthyroidism, diabetes, prostatic hypertrophy, hypertension, arrhythmias
Adverse Effects	Tachycardia, palpitations, nervousness, excitability, insomnia, tremor
Drug Interactions	Do not use with MAO inhibitors. May increase the effects of bromocriptine and other sympathomimetics. Effects may be increased by antacids, atomoxetine, cannabinoids, carbonic anhydrase inhibitors, serotonin/norepinephrine reuptake inhibitors. Effects may be decreased by spironolactone.
Monitoring	Heart rate, blood pressure (if patient has a history of hypertension)
Case Notes	Pseudoephedrine and phenylephrine are both available over-the-counter for the treatment of sinus congestion. Pseudoephedrine is typically only sold by pharmacy personnel and may only be bought in limited supply due to the ability to use the tablets to manufacture methamphetamine. The regulation of pseudoephedrine sales is determined by individual state governments. Systemic decongestants have shown marginal effectiveness in treatment of congestion due to infections and are not recommended in children less than 6 years of age. Unintentional overdoses in children have led to hospitalizations and deaths. Single-ingredient over-the-counter products that target patient-specific symptoms should be recommended rather than multiple-ingredient products. Topical adrenergic agonists include naphazoline, oxymetazoline, and phenylephrine. Topical agents should be used for no more than three days to avoid rebound congestion (rhinitis medicamentosa).

A 42-year-old man presents to the pharmacy to pick up a prescription refill. While paying for his prescription, he asks if you have a recommendation for something he can take for a cough. He has had a cough and runny nose for two days and has been using diphenhydramine. It has helped his runny nose, but his cough persists. His past medical history is significant for hypercholesterolemia.

Allergies: NKDA

Medications: Atorvastatin 40 mg tablet 1 po once daily; diphenhydramine 25 mg tablet (OTC) 1 po every 6 hours

What over-the-counter product would you recommend for this patient to help with his cough?

Dextromethorphan	Antitussive
Mechanism of Action	Controls cough by depressing the medullary cough center
***Contraindications*/ Precautions**	*Hypersensitivity, use within 14 days of MAO inhibitors*/Persistent cough, cough with excessive secretions, potential for abuse
Adverse Effects	Rare in recommended doses, but may cause nausea, drowsiness, or dizziness. In overdose, may cause mental status changes.
Drug Interactions	Do not use with MAO inhibitors or sibutramine. Dextromethorphan is a major substrate of CYP2D6. Use with 2D6 inhibitors increases the adverse effect potential of dextromethorphan.
Monitoring	Cough, mental status
Case Notes	In clinical trials, dextromethorphan has failed to show significant reduction in cough, but is relatively safe to use and may be recommended for patients with a cough that has been present for less than one week and is not productive. Any patients with asthma should be counseled to speak with their physician when they have a cough rather than using antitussive medications. Dextromethorphan is chemically related to morphine and does have the potential for abuse in large doses. Single-ingredient over-the-counter products that target patient-specific symptoms should be recommended.

The mother of a 9-month-old girl presents to the pharmacy for advice. Her daughter was diagnosed with respiratory syncytial virus (RSV) three days ago by her physician. At that time she had a fever and occasional cough. Over the last two days, her nasal congestion has increased. She continues to eat well and does not seem irritable. She has no other medical conditions.

Allergies: NKDA

Medications: None

What would you recommend for this patient to help with her nasal congestion?

Intranasal Sodium Chloride	Sodium
Mechanism of Action	Increases moisture in nasal membranes
***Contraindications/* Precautions**	*Hypersensitivity to sodium chloride*
Adverse Effects	None
Drug Interactions	None
Monitoring	Nasal congestion, ability to eat, drink, and sleep
Case Notes	RSV is a self-limiting infection for which there is no treatment except supportive care. Supportive care typically includes adequate fluid intake, use of a cool-mist humidifier, and decreasing nasal mucus with the use of saline. Since this patient continues to eat well and does not have excessive irritability, self-care is appropriate. Intranasal saline is available over the counter as a 0.65% solution and is the first choice for nasal congestion in children younger than 6. For children younger than 2, nasal drops are preferred to sprays and should be followed by bulb suctioning of the nostrils to remove mucus. Intranasal saline should be used before the infant eats and sleeps, up to four to six times a day. Over-the-counter systemic decongestant products are not recommended for children younger than 6 years of age and would not be expected to provide a significant benefit for RSV symptoms. Topical phenylephrine may be used in children >6 months of age if intranasal saline is not effective. Antihistamines and cough suppressants are also not recommended for use in pediatric viral infections.

A 7-year-old is being evaluated in the pulmonary clinic. He has just been diagnosed with cystic fibrosis with a positive sweat chloride test. He has been diagnosed with pneumonia four times in the past two years, and he was diagnosed with asthma three years ago. He complains that he coughs daily and his cough is often productive.

Allergies: Sulfamethoxazole/trimethoprim (rash)

Medications: Budesonide 180 mcg flexhaler 1 puff twice daily; albuterol HFA 90 mcg 2 puffs with spacer PRN

Physical Exam/Other Studies:

Wt 40 lb (<5th percentile) Ht 45 in (10th percentile) T 98.9°F BP 98/62 HR 92 RR 17
O_2 sat 97%

Physical exam reveals a thin male in no apparent distress. He has mild digital clubbing. Lung exam reveals diffuse crackles.

Spirometry reveals an FEV_1 of 72% predicted and an FVC of 92% predicted. Neither value is significantly changed after administration of albuterol.

Sputum culture: methicillin-sensitive *Staphylococcus aureus*

The patient will be started on cephalexin for 21 days to determine if any improvement in his lung function will occur. What other medication would you recommend to help maintain this patient's lung health?

Dornase Alfa	Inhalational enzyme and mucolytic
Mechanism of Action	Selectively cleaves DNA, reducing mucus viscosity to improve airflow and decrease the risk of bacterial infections
Contraindications/ **Precautions**	*Hypersensitivity to dornase alfa or Chinese hamster ovary cell products*
Adverse Effects	Sore throat, dyspepsia, conjunctivitis, cough, hemoptysis, laryngitis, pharyngitis, voice alteration, hoarseness. Fever occurs more commonly in patients with FVC <40% predicted.
Drug Interactions	Should not be mixed with other medications in the nebulizer as this may inactivate the dornase
Monitoring	Pulmonary function tests
Case Notes	Pulmonary consensus guidelines from the Cystic Fibrosis Foundation recommend the use of dornase alfa in any patient 6 years of age and older with pulmonary symptoms and is continued for life. Dornase alfa has been studied in infants as young as 3 months of age and in clinical practice is often used at the onset of pulmonary symptoms regardless of age. The dose is 2.5 mg (one single-use vial) in the nebulizer once a day. Dornase alfa is stored in the refrigerator and is often a special order item for pharmacies. This patient should also start chest percussion therapy (CPT) twice a day to help facilitate mucus removal from the lungs. Whether dornase alfa should be given before or after CPT is not well studied and is controversial. For patients colonized with *Staphylococcus aureus*, routine antibiotic administration is not recommended. These patients are treated with 14-21 days of antibiotics during times of increased symptoms known as pulmonary exacerbations.

A 24-year-old is being seen for a follow-up visit in the pulmonary clinic. She was diagnosed with cystic fibrosis shortly after birth. She has no new complaints at this visit and feels she is at her baseline, which includes infrequent cough during the day. She completed a three-week course of ciprofloxacin one week ago.

Allergies: Penicillin (hives and shortness of breath), ceftazidime (rash)

Medications: Pancrelipase 24,000 units lipase per capsule 4 capsules po with meals and 2 with snacks; fat-soluble vitamin supplement 2 tablets po once daily; dornase alfa 2.5 mg nebulized once daily; lansoprazole 30 mg capsule 1 po once daily; azithromycin 500 mg tablet 1 po on Monday, Wednesday, and Friday

Physical Exam/Other Studies:

Wt 125 lb Ht 65 in T 98.2°F BP 112/74 HR 81 RR 12 O_2 sat 97%

Physical exam reveals mild digital clubbing. Lung exam reveals sporadic crackles.

Sputum culture: *Pseudomonas aeruginosa.* Prior to three months ago, she had not had any cultures positive for *Pseudomonas*. Monthly cultures since then have been *Pseudomonas* positive.

What inhaled medication is recommended for patients with cystic fibrosis who are colonized with *Pseudomonas aeruginosa*?

Inhaled Tobramycin	Inhaled aminoglycoside antibiotic
Mechanism of Action	Binds to 30S and 50S ribosomal subunits, resulting in defective bacterial cell membrane.
***Contraindications*/ Precautions**	*Hypersensitivity to tobramycin*/Pre-existing renal, auditory, or vestibular impairment
Adverse Effects	Voice alteration, bronchospasm, dyspnea, cough, pharyngitis, hoarseness. Rarely, systemic concentrations of inhaled tobramycin are detectable.
Drug Interaction	Should not be mixed with dornase alfa in the nebulizer
Monitoring	Pulmonary function, renal function; may consider a one-hour post level to identify the minority of patients with detectable levels
Case Notes	Pulmonary consensus guidelines from the CF Foundation recommend using inhaled tobramycin in patients 6 years of age and older who are colonized with *Pseudomonas aeruginosa* (PA) regardless of lung function and symptoms. Studies are available for use in younger patients, and in clinical practice, younger patients colonized with PA are typically started on inhaled tobramycin. Inhaled tobramycin is given as a 300 mg unit dose vial in the nebulizer twice a day, every other month. Once started, it is not discontinued unless the patient experiences intolerable adverse effects. Inhaled tobramycin is also used in PA eradication regimens where it is administered for one to three months in patients who have a new acquisition of PA. In 2010, inhaled aztreonam was also approved for use in patients with CF colonized with PA. Studies are needed to determine which medication should be considered first line. At this time, more long-term data are available for tobramycin, making it the first choice in patients without contraindications. Azithromycin three days weekly is also recommended to reduce inflammation in those with CF who are colonized with PA.

A 7-year-old is being evaluated in the pulmonary clinic. He has just been diagnosed with cystic fibrosis with a positive sweat chloride test. He has been diagnosed with pneumonia four times in the past two years, and he was diagnosed with asthma three years ago. He complains that he coughs daily and his cough is often productive. He also complains that he has runny stools that are foul smelling and occur up to six times a day.

Allergies: Sulfamethoxazole/trimethoprim (rash)

Medications: Budesonide 180 mcg flexhaler 1 puff twice daily; albuterol HFA 90 mcg 2 puffs with spacer PRN

Physical Exam/Other Studies:

Wt 40 lb (<5th percentile) Ht 45 in (10th percentile) T 98.9°F BP 98/62 HR 92 RR 17
O_2 sat 97%

Physical exam reveals a thin male in no apparent distress. He has mild digital clubbing. Lung exam reveals diffuse crackles.

Spirometry reveals an FEV_1 of 72% predicted and an FVC of 92% predicted. Neither value is significantly changed after administration of albuterol.

Sputum culture: methicillin-sensitive *Staphylococcus aureus*

What medication would you recommend to help increase his weight and normalize his bowel movements?

Pancreatic Enzyme Supplement	Various name brand products containing lipase, amylase, and protease
Mechanism of Action	Replaces pancreatic enzymes to assist in digestion of protein, starch, and fats
***Contraindications*/ Precautions**	*Hypersensitivity to bovine or pork protein, acute exacerbations of chronic pancreatic diseases, acute pancreatitis*/Powder is a skin and pulmonary irritant
Adverse Effects	Nausea, abdominal cramps, constipation, colonic stricture (with higher than recommended doses), perianal irritation, hyperuricemia
Drug Interactions	Calcium carbonate and magnesium hydroxide may decrease enzyme effectiveness; enzymes may decrease the response to oral iron therapy; agents that decrease gastric acid increase enzyme effectiveness.
Monitoring	Stool frequency and consistency, weight, serum vitamin concentrations
Case Notes	The majority of patients with CF are pancreatic insufficient and will require pancreatic enzyme replacement. Dosing is based on the lipase content, and a child of this age is started at 500 units of lipase/kg/meal with half of that amount given with snacks. This patient's dose would be calculated at 9,090 units of lipase/meal. The closest available capsule size would be 10,000 units per capsule. A 5,000 unit capsule could be used with snacks. The capsules can be swallowed whole or opened and the contents sprinkled on a small amount of soft food. The dose is titrated up every one to two weeks depending on clinical response. There are subtle differences between the products, and switching from one product to another may change a patient's clinical response. Doses should not exceed 2,500 units/kg/meal or 10,000 units/kg/day when possible to avoid the risk of colonic strictures. For many patients, the addition of acid-suppressive therapy is necessary for adequate function of the enzyme replacement product. Powder or tablet products that are not microencapsulated are only recommended in patients unable to take any medication by mouth such as patients who are intubated.

A 29-year-old woman presents to her physician complaining that her asthma is getting worse. She was diagnosed with asthma as a child, but for the past 20 years has been controlled on albuterol as needed alone. She has noticed that over the past month, she has begun having a cough two to three days a week, and felt slightly short of breath once in the past week. She had one episode of shortness of breath while she was sleeping about three weeks ago. She has used her albuterol about three times per week in the past month. Each time she uses albuterol, it relieves her symptoms. She is currently 27 weeks pregnant.

Allergies: NKDA

Medications: Prenatal vitamin tablet 1 po once daily; albuterol HFA 90 mcg 2 puffs with spacer PRN

Physical Exam/Other Studies:

Wt 143 lb Ht 67 in T 98.7°F BP 121/79 HR 92 RR 13 O_2 sat 99%

Physical exam reveals no significant findings.

Which inhaled corticosteroid has a pregnancy risk factor rating of B?

Budesonide	Inhaled corticosteroid (beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone)
Mechanism of Action	Decreases neutrophil migration and reverses capillary permeability to prevent or control inflammation
***Contraindications*/ Precautions**	*Hypersensitivity*/If high doses are used, HPA suppression, reduction of growth velocity, or decreased bone mineral density may occur.
Adverse Effects	Oral thrush, dry mouth, taste alteration, pharyngitis, cough, hoarseness. Rarely, glaucoma or cataracts have been reported. Adverse effects mimic those of systemic steroids when used in high doses.
Drug Interactions	CYP3A4 substrate. Levels may increase in the presence of a CYP3A4 inhibitor, increasing the rate of adverse effects.
Monitoring	Mucus membranes, pulmonary function, asthma control
Case Notes	According to the NIH working group on managing asthma in pregnancy guidelines published in 2004, the preferred inhaled corticosteroid during pregnancy is budesonide. None of the inhaled corticosteroids have been linked to fetal abnormalities when used during pregnancy, but budesonide has the largest number of studies involving pregnant women. The benefits to the fetus of maternal asthma control outweigh any potential risk of asthma therapies. The working group also states that if a patient is currently controlled on an inhaled corticosteroid other than budesonide, the patient does not need to change to budesonide. This patient's asthma would be classified as mild persistent, warranting treatment with a low-dose inhaled corticosteroid. She should receive 180-600 mcg of budesonide daily.

The mother of a 3-year-old boy presents to the pharmacy to pick up a refill prescription for her son. The prescription is for albuterol nebulizer solution and has been refilled every month for the past three months. Upon questioning, you find out that he has a cough every night while sleeping and a cough during the day almost every day. He continues to play with other kids, but occasionally has to stop because he is breathing hard. His mom is giving him albuterol at least three times a day, which she believes improves his cough.

Allergies: NKDA

Medications: None

Physical Exam/Other Studies:

Not available

What type of medication would you recommend the physician prescribe for this patient?

Inhaled Corticosteroid	Beclomethasone, budesonide, ciclesonide, flunisolide, fluticasone, mometasone
Mechanism of Action	Decreases neutrophil migration and reverses capillary permeability to prevent or control inflammation
***Contraindications*/ Precautions**	*Hypersensitivity*/If high doses are used, HPA suppression, reduction of growth velocity, or decreased bone mineral density may occur.
Adverse Effects	Oral thrush, dry mouth, taste alteration, pharyngitis, cough, hoarseness. Rarely, glaucoma or cataracts have been reported. Adverse effects mimic those of systemic steroids when used in high doses.
Drug Interactions	CYP3A4 substrate. Levels may increase in the presence of a CYP3A4 inhibitor, increasing the rate of adverse effects.
Monitoring	Growth (in pediatric patients), mucus membranes, asthma control
Case Notes	According to the NIH guidelines from 2007, this patient's asthma would be classified as severe, necessitating step 3 therapy of a medium-dose inhaled corticosteroid. Inhaled corticosteroids that are recommended for children this age include fluticasone metered dose inhaler or budesonide nebulizer solution. If fluticasone is chosen, a spacer with mask should be used to administer the medication until 5-6 years of age. Appropriate dosing for fluticasone would be 110 mcg one puff twice daily. Budesonide would be dosed at 0.5 mg twice daily. This patient may also benefit from the use of a short course of oral steroids to gain faster symptom control. Inhaled steroids delivered using a spacer with mask have been shown to be effective in children as young as 6 months of age. Using an inhaler with spacer is usually more convenient, less time consuming, and more cost effective than nebulization. The choice of an inhaler or nebulizer should consider patient and caregiver preferences.

A 16-year-old boy presents to the pediatric clinic for an asthma follow-up. He reports that he wakes up coughing once or twice a week and coughs during the day about once a week. He is able to participate in physical activity, but has some difficulty breathing when running for a long period of time. He uses his albuterol about three times each week. He also has seasonal allergies, which are currently well controlled. He reports taking his medications daily as prescribed.

Allergies: NKDA

Medications: Cetirizine 10 mg tablet (OTC) 1 po once daily; fluticasone HFA 220 mcg 1 puff with spacer twice daily; albuterol HFA 90 mcg 2 puffs with spacer PRN

Physical Exam/Other Studies:

Wt 170 lb Ht 72 in T 98.9°F BP 112/65 HR 62 RR 12 O_2 sat 99%

Physical exam reveals a prolonged expiratory phase on the respiratory exam.

Asthma Control Test: 17

What type of medication would you recommend for this patient?

Long-Acting Beta$_2$-Agonist	Salmeterol and formoterol; arformoterol for COPD only
Mechanism of Action	Beta$_2$-agonists stimulate beta$_2$-adrenergic receptors, leading to smooth muscle relaxation and mast cell stabilization.
***Contraindications*/ Precautions**	*Hypersensitivity*/Patients with coronary insufficiency, hypertension, arrhythmia. In some patients, long-acting beta$_2$-agonists (LABAs) may be associated with a worsening of asthma severity and an increase in asthma-related mortality.
Adverse Effects	Tachycardia, hypertension, nervousness, hyperactivity, insomnia, dizziness, tremor, headache
Drug Interactions	Less effective when used with beta-adrenergic blockers. Cardiovascular effects may be potentiated in patients on sympathomimetics, tricyclic antidepressants, MAO inhibitors. May decrease digoxin serum levels.
Monitoring	Heart rate, respiratory rate, blood pressure, asthma control
Case Notes	This patient's asthma would be classified as "not well controlled" on a medium-dose inhaled corticosteroid. According to the NIH guidelines from 2007, addition of an LABA is the preferred action at this time. Appropriate products include: fluticasone/salmeterol, budesonide/formoterol, or mometasone/formoterol. Fluticasone/salmeterol could be provided as either a 250/50 mcg dry powder inhaler 1 puff twice daily or the 115/21 mcg metered dose inhaler (MDI) 2 puffs twice daily. Budesonide/formoterol would be 160/4.5 mcg MDI 2 puffs twice daily, and mometasone/formoterol would be 100/4.5 mcg MDI 2 puffs twice daily. An alternative to an LABA would be a leukotriene modifier. While this is not the preferred therapy, it may be considered in those intolerant to or concerned about the use of LABAs. Another alternative is to increase the inhaled steroid to high dose. Because of the concern of a potential increase in asthma morbidity and mortality, in 2010 the FDA issued an alert that LABAs should only be used if inhaled corticosteroids do not adequately control asthma symptoms.

A 32-year-old woman presents to the clinic for an asthma evaluation. She reports that her asthma was well controlled until about one week ago when the season started changing. She had cough and shortness of breath two mornings in the past week for which she has taken albuterol. She also reports that she has increased nasal drainage. Her past medical history is significant for allergic rhinitis, asthma, and atrial fibrillation. She reports good adherence to her medication regimen.

Allergies: Penicillin (rash)

Medications: Warfarin 1 mg tablet 1 po once daily; loratadine 10 mg tablet (OTC) 1 po once daily; fluticasone nasal spray 1 spray in each nostril twice daily; fluticasone HFA 220 mcg 1 puff twice daily; albuterol HFA 90 mcg 2 puffs with spacer PRN

Physical Exam/Other Studies:

Wt 190 lb Ht 65 in T 98.9°F BP 131/82 HR 84 RR 10 O_2 sat 98%

Occasional end-expiratory wheezing that cleared after 2 puffs of albuterol

What medication would you recommend for this patient to better control her asthma?

Montelukast	Leukotriene modifier (montelukast, zafirlukast, zileuton)
Mechanism of Action	Montelukast and zafirlukast are leukotriene receptor antagonists and thus decrease leukotriene-induced bronchospasm, vascular permeability, mucosal edema, and mucus production. Zileuton is a 5-lipoxygenase inhibitor that inhibits leukotriene formation.
***Contraindications*/ Precautions**	*Hypersensitivity*/Avoid chewable tablets in patients with phenylketonuria. May be associated with neuropsychiatric events, including aggression, anxiousness, hallucinations, insomnia, and suicidal ideations. Patients with active liver disease should not start zafirlukast or zileuton.
Adverse Effects	Abdominal pain, dyspepsia, headache, elevated liver enzymes, sinusitis. The risk for hepatitis is higher for zafirlukast and zileuton compared to montelukast. May be associated with neuropsychiatric events including aggression, anxiousness, hallucinations, insomnia, and suicidal ideations.
Drug Interactions	Phenobarbital and rifampin may decrease montelukast concentrations. Zafirlukast is a CYP3A4 isoenzyme inhibitor. Zileuton is a CYP1A2 isoenzyme inhibitor.
Monitoring	Neuropsychiatric state, asthma control
Case Notes	According to the NIH guidelines from 2007, this patient's asthma is not well controlled on a medium-dose inhaled corticosteroid and a step up in therapy is indicated. The addition of a long-acting beta$_2$-agonist is typically preferred, but should be used cautiously in patients with arrhythmias. Also, the addition of a leukotriene modifier may help improve her allergy symptoms. Montelukast 10 mg once daily would be the agent of choice because both zafirlukast and zileuton may decrease warfarin metabolism. Another alternative is to increase the inhaled corticosteroid to high dose. If the addition of montelukast has not been beneficial within two months, it should be discontinued.

A 24-year-old woman presents to the Internal Medicine clinic complaining of cough and shortness of breath with exercise. She started jogging a month ago and reports that about 5-10 minutes after starting, she begins to cough and have trouble breathing. She often has to stop jogging to catch her breath. The symptoms resolve about 10-20 minutes after she stops. She reports that these symptoms do not occur at any other time during the day or night but remembers an episode in the fall where she woke up with a cough and trouble breathing. Her past medical history is significant for migraine headaches and asthma as a child. She reports that she grew out of her asthma when she was about 8 years old. She does not smoke and drinks two to three alcoholic beverages per week.

Allergies: NKDA

Medications: Sumatriptan 25 mg tablet 1 po PRN migraine

Physical Exam/Other Studies:

Wt 132 lb Ht 66 in T 98.6°F BP 124/73 HR 75 RR 12 O_2 sat 99%

Physical exam reveals no pertinent findings.

ECG is normal.

Spirometry before and after six minutes of jogging on a treadmill: FEV_1 was 94% of predicted before jogging and 76% of predicted after jogging. FVC was unchanged at 98% of predicted.

What type of medication would you recommend for this patient?

Inhaled Short-Acting Beta$_2$-Agonist	Albuterol, pirbuterol, and levalbuterol
Mechanism of Action	Beta$_2$-agonists stimulate beta$_2$-adrenergic receptors, which leads to smooth muscle relaxation and mast cell stabilization.
***Contraindications*/ Precautions**	*Hypersensitivity to any beta$_2$-agonist*/Coronary insufficiency, hypertension, arrhythmia
Adverse Effects	Tachycardia, hypertension, nervousness, hyperactivity, insomnia, dizziness, tremor, hypokalemia. Long-term frequent administration results in down regulation of beta receptors.
Drug Interactions	Less effective when used with beta-adrenergic blockers. Cardiovascular effects may be potentiated in patients on sympathomimetics, tricyclic antidepressants, MAO inhibitors. May decrease digoxin serum levels.
Monitoring	Heart rate, respiratory rate, blood pressure. Monitor potassium with administration of high doses or prolonged use.
Case Notes	This patient's asthma severity would be classified as mild intermittent and a short acting beta$_2$ agonist is recommended. Inhaler technique should be observed. Use of a spacer with metered dose inhalers is recommended to improve technique and decrease systemic absorption. Use two puffs 5-30 minutes before exercise. The dose may be repeated if symptoms occur during the activity. Pirbuterol is a breath-actuated metered dose inhaler that does not require the use of a spacer. Levalbuterol is the R-enantiomer of albuterol. It has not been shown to be more effective than albuterol and is more costly. It may be associated with a lower risk of tremor compared to albuterol. If a patient is not able to tolerate short-acting beta$_2$-agonists, a mast cell stabilizer, such as cromolyn or nedocromil, may be used prior to exercise.

A 52-year-old woman presents to the emergency department due to an asthma exacerbation. She began having trouble a week ago after going to a bar where there was cigarette smoke. She has been using her albuterol inhaler every two hours for three days. In the emergency room, she has been given three doses of albuterol 5 mg by nebulizer and ipratropium 0.5 mg by nebulizer.

Allergies: NKDA

Medications: Budesonide/formoterol 160/4.5 mcg MDI 2 puffs twice daily; albuterol HFA MDI 90 mcg 2 puffs with spacer PRN; enalapril 10 mg tablet 1 po once daily

Physical Exam/Other Studies:

Wt 152 lb Ht 67 in T 98.9°F BP 135/92 HR 110 RR 26 O_2 sat 87%

She appears to be in distress and is having difficulty talking. She has intercostal retractions and decreased air entry with inspiratory and expiratory wheezing.

What medication would you recommend for this patient?

Prednisone	Oral systemic corticosteroid (prednisone, prednisolone, methylprednisolone, dexamethasone)
Mechanism of Action	Decreases neutrophil migration and reverses capillary permeability to prevent or control inflammation
***Contraindications/* Precautions**	*Serious infections (except septic shock or tuberculosis), systemic fungal infections, varicella infections, administration with live vaccines*/Hyperglycemia, tuberculosis, untreated systemic infections, thyroid dysfunction, hypertension, osteoporosis, thromboembolic tendency, peptic ulcer
Adverse Effects	Effects with short- or long-term use include edema, hypertension, psychoses, insomnia, headache, impaired wound healing, bruising, hyperglycemia, weight gain, increased appetite, nausea, vomiting, muscle weakness, immunosuppression. Effects seen primarily with long-term or frequent use include HPA suppression, Cushing's syndrome, growth suppression, peptic ulcer, decreased bone mineral density, fractures, cataracts, glaucoma.
Drug Interactions	CYP3A4 substrate and inducer. Levels may increase in the presence of a CYP3A4 inhibitor, increasing the rate of adverse effects.
Monitoring	Blood pressure, weight, blood glucose
Case Notes	This patient is having an asthma exacerbation that has not responded to albuterol and ipratropium; therefore, a systemic steroid is indicated. The oral route should be used in patients who are able to swallow. The recommended dose for adults is 40-80 mg daily in one or two doses a day for 3-10 days or until symptoms resolve. The recommended dose for children is 1-2 mg/kg/day, up to 60 mg daily. Systemic steroid doses do not need to be tapered if used for 14 days or less. Prednisone is the most commonly used tablet, and prednisolone is the recommended liquid formulation. Dexamethasone has the longest duration of action of two to three days and has no mineralocorticoid activity. Methylprednisolone also has no mineralocorticoid activity.

A 22-year-old woman presents to the pulmonologist for an asthma evaluation. She is recovering from an exacerbation for which she has been on prednisone for three days. Her asthma symptoms keep her from participating in physical activity and often keep her from sleeping at night. She has been hospitalized six times in the past year for asthma and was mechanically ventilated during one of those visits. She has made every environmental modification that has been recommended to her. She does not smoke or have exposure to tobacco smoke. She reports good adherence to her medication regimen. Last year, she tried theophylline but did not tolerate the side effects. Her medical history includes allergic rhinitis and recurrent sinusitis.

Allergies: Penicillin (hives), sulfamethoxazole/trimethoprim (hives), peanuts (anaphylaxis)

Medications: Montelukast 10 mg tablet 1 po once daily; fluticasone/salmeterol 500/50 mcg diskus 1 puff twice daily; cromolyn 20 mg/2 mL nebulizer solution 1 vial three times daily; cetirizine 10 mg tablet (OTC) 1 po once daily; mometasone nasal spray 2 sprays in each nostril once daily; prednisone 20 mg tablet 2 po twice daily for 7 more days

Physical Exam/Other Studies:

Wt 124 lb Ht 63 in T 99°F BP 115/71 HR 84 RR 14 O_2 sat 98%

Expiratory wheezes in all lung fields. Prolonged expiratory phase.

IgE 632 kU/L (<114 kU/L)

What additional medication may be recommended by the pulmonologist at this time?

Omalizumab	Monoclonal antibody
Mechanism of Action	IgG monoclonal antibody that binds to free IgE and prevents binding of IgE to the receptor on the surface of mast cells and basophils. This decreases the early- and late-phase allergic response.
Contraindications/ **Precautions**	*Hypersensitivity to omalizumab*/Patients at risk for geohelminthic infections
Adverse Effects	Hot flashes, headache, dizziness, fatigue, urticaria, injection site reactions (within one hour and lasting up to eight days), arthralgia, wheezing. Rarely thrombocytopenia and alopecia. Acute and delayed anaphylaxis may occur within 2-24 hours after administration. Occasionally reactions have occurred >24 hours after. Medication should be administered under medical supervision and be observed for at least two hours.
Drug Interactions	None observed
Monitoring	Baseline total serum IgE, pulmonary function tests, hypersensitivity reactions
Case Notes	Omalizumab is recommended when asthma is not adequately controlled with other therapies. It is given subcutaneously at a dose and frequency determined by the baseline IgE level and patient weight. For this patient's IgE (>600 kU/mL) and weight (30-60 kg), the recommended dose is 375 mg every two weeks. For patients with this IgE level and a weight over 60 kg, omalizumab is not recommended because dosing has not been established. Total IgE levels remain elevated during treatment and for a year after discontinuation; thus remeasurement of IgE levels is not recommended. Response to therapy is expected to take 12-16 weeks. Patients should be trained on the management of anaphylaxis in the home. Omalizumab is supplied in a 150 mg single-use vial that, once reconstituted, is stable for four hours at room temperature and eight hours in the refrigerator.

A 44-year-old woman presents to her PCP's office because of previous suspicion that she may have rheumatoid arthritis (RA). Three months ago, she presented with very nonspecific joint pain in her hands and was given an NSAID to see if it would help. Over the last two months, her condition has worsened. She now has visible swelling and redness of the proximal interphalangeal (PIP) joints of her hands, bilaterally, with swelling and redness at both wrists as well. Her joints remain stiff in the morning for about one hour. She feels fatigued during the day, especially in the afternoon.

Allergies: NKDA

Medications: Ibuprofen 600 mg tablet 1 po three times daily

Physical Exam/Other Studies:

Wt 150 lb Ht 66 in T 98.6°F BP 122/74 HR 84 RR 12 O_2 sat 99%

Physical exam reveals two swollen and erythematous PIP joints bilaterally, swollen and erythematous wrists.

CRP 65 mg/L ESR 60 mm/hr

Rheumatoid factor: +

Anticyclic citrullinated peptide: +

X-ray shows soft tissue swelling around PIP joints and possible joint-space narrowing.

The PCP determines that the patient has RA and wants to start a disease-modifying antirheumatic drug (DMARD).

What is the first-line DMARD of choice to treat rheumatoid arthritis?

Methotrexate	Disease-modifying antirheumatic drug (DMARD); antineoplastic
Mechanism of Action	In RA, specific action is unknown, but may affect immune function; folate antagonist
***Contraindications*/ Precautions**	*Hypersensitivity, pregnancy, breastfeeding, alcoholism, liver disease, blood dyscrasias, immunodeficiency syndrome*/May cause renal failure, hepatotoxicity, bone marrow suppression, severe dermatologic reactions, oligospermia, menstrual dysfunction, malignant lymphomas, neurotoxicity, immunosuppression, opportunistic infections, pneumonitis; use caution in renal or hepatic impairment; use with NSAIDs may cause severe bone marrow suppression, aplastic anemia, and GI toxicity
Adverse Effects	Ulcerative stomatitis, glossitis, gingivitis, nausea, vomiting, diarrhea, leukopenia, renal failure, myelosuppression, thrombocytopenia, reddening of skin, rash, photosensitivity, dizziness, seizure, encephalopathy, fever, chills, vasculitis, arthralgia, blurred vision, pneumonitis, hepatic impairment, hyperuricemia, defective oogenesis or spermatogenesis
Drug Interactions	NSAIDs, salicylates, probenecid, sulfonamides; see product labeling for multiple interactions; avoid use with acitretin, natalizumab, pimecrolimus, tacrolimus, or live vaccines
Monitoring	CBC with differential and platelets, serum creatinine, and LFTs (baseline, then every two to four weeks for initial three months; then every 8-12 weeks for three to six months; and then every 12 weeks after six months); chest x-ray (baseline); pulmonary function test (if methotrexate-induced lung disease suspected); hepatitis B or C testing (baseline)
Case Notes	Methotrexate is as effective as, and often has a quicker onset of action than, other DMARDs. Methotrexate is often used as the first-line agent, but sulfasalazine or leflunomide may be used as well. Long-term data suggest methotrexate has superior outcomes over other DMARDs. Oral dose: 7.5 mg once weekly or 2.5 mg every 12 hours for three doses/week; maximum of 20-25 mg/week. IM dose: 5-25 mg/week. Folic acid 5 mg/week may reduce some adverse effects.

A 48-year-old woman presents to her PCP's office for a follow-up visit of her rheumatoid arthritis (RA). Her past medical history includes Type 2 diabetes with retinopathy. She has been taking methotrexate for eight months, and while it has improved her symptoms, she is not completely satisfied with its effectiveness. Currently, she has visible swelling and redness of the proximal interphalangeal (PIP) joints of her hands, bilaterally. Her joints remain stiff in the morning for about 80 minutes, and she feels fatigued often. She has tried to take sulfasalazine for RA, but cannot tolerate its GI effects. Her vision is poor due to diabetic retinopathy.

Allergies: NKDA

Medications: Methotrexate 10 mg tablet 1 po weekly; insulin glargine inject 24 units subcutaneously daily; ramipril 5 mg capsule 1 po daily

Physical Exam/Other Studies:

Wt 178 lb Ht 66 in T 98.6°F BP 126/78 HR 76 RR 14

Physical exam reveals two swollen and erythematous PIP joints bilaterally.

LFT: normal

CBC: normal

X-ray shows soft tissue swelling around PIP joints and joint-space narrowing.

The PCP would like to add another disease-modifying antirheumatic drug (DMARD) to her methotrexate. The PCP chooses to avoid hydroxychloroquine due to risks of further vision impairment.

What traditional (nonbiologic) DMARD may be added to her current RA regimen?

Leflunomide	Disease-modifying antirheumatic drug (DMARD)
Mechanism of Action	Inhibits pyrimidine synthesis, resulting in antiproliferative and anti-inflammatory effects
***Contraindications*/ Precautions**	*Hypersensitivity, pregnancy*/May cause dermatologic reactions, hepatotoxicity, malignancy, immunosuppression, infections, interstitial lung disease; caution if history of hematologic diseases, tuberculosis; not recommended in hepatic disease; women of childbearing potential should not receive therapy until pregnancy has been excluded and they have been counseled concerning fetal risk and reliable contraceptive measures have been confirmed.
Adverse Effects	Diarrhea, respiratory tract infection, hypertension, chest pain edema, headache, dizziness, fever, malaise, alopecia, rash, nausea, abdominal pain, dyspepsia, weight loss, stomatitis, anemia, urinary tract infection, abnormal LFT, cholelithiasis, anemia, back pain, joint disorder, eye disorder, pneumonia, cough, bronchitis
Drug Interactions	Inhibits CYP2C9; bile acid sequestrants, warfarin, immunosuppressants; see labeling for multiple interactions; avoid use with natalizumab, pimecrolimus, tacrolimus, or live vaccines
Monitoring	CBC with differential and platelets, serum creatinine, and LFTs (baseline, then every month for five months, then every one to two months); infections; pregnancy, hepatitis B or C testing (baseline)
Case Notes	While methotrexate is often the initial DMARD of choice, leflunomide, sulfasalazine, and/or hydroxychloroquine may be added to improve efficacy. Biologic agents may be used next in therapy. Leflunomide is teratogenic; following treatment, pregnancy should be avoided until undetectable serum concentrations (<0.02 mg/L) are verified (may take two years); this may be accomplished by the use of an enhanced drug elimination procedure using cholestyramine. Serum concentrations <0.02 mg/L should be verified by two separate tests performed at least 14 days apart. Oral dose: 100 mg/day for three days, followed by 20 mg/day (if not tolerated, 10 mg/day).

A 45-year-old woman presents to her PCP's office for a follow-up visit of her rheumatoid arthritis (RA). She has been taking a combination of methotrexate, hydroxychloroquine, and sulfasalazine without gaining remission or significant improvement of her RA. She complains of swollen joints and morning stiffness. She would like to try a new treatment.

Allergies: NKDA

Medications: Methotrexate 7.5 mg tablet 1 po weekly; hydroxychloroquine 200 mg tablet 2 po daily; sulfasalazine 500 mg tablet 2 po twice daily

Physical Exam/Other Studies:

Wt 130 lb Ht 65 in T 98.6°F BP 114/74 HR 72 RR 12

Physical exam reveals two swollen and erythematous PIP joints bilaterally.

The PCP would like to switch her therapy from oral DMARDs to a biologic agent.

Which of the following is the most appropriate biologic agent to use initially for this patient's RA?

A. rituximab
B. abatacept
C. anakinra
D. etanercept

Etanercept	Biologic disease-modifying antirheumatic drug (DMARD); tumor necrosis factor (TNF) blocker
Mechanism of Action	A recombinant DNA-derived protein composed of a TNF receptor linked to the Fc portion of human IgG1 that binds TNF and blocks its interaction with cell surface receptors; decreases the inflammatory process
***Contraindications/* Precautions**	*Hypersensitivity, sepsis/*May cause or increase risk of infections, malignancy, reactivation of hepatitis B, autoimmune disorder, anaphylaxis, tuberculosis (TB); caution if history of alcoholic hepatitis, demyelinating CNS disease, heart failure, hematologic disorders, Wegener's granulomatosis; not recommended if taking anakinra or if exposed to varicella
Adverse Effects	Headache, abdominal pain, vomiting, injection site reaction, respiratory tract infection, infection, dizziness, rash, nausea, dyspepsia, weakness, cough
Drug Interactions	Denosumab, leflunomide, sipuleucel-T, echinacea; avoid use with anakinra, abatacept, canakinumab, certolizumab pegol, natalizumab, cyclophosphamide, pimecrolimus, tacrolimus, rilonacept, and live virus vaccines
Monitoring	Latent TB screening prior to therapy initiation; signs and symptoms of infection
Case Notes	A tumor necrosis factor (TNF-α) inhibitor should be the first biologic used; any of the other options could be used once a TNF-α inhibitor has failed. Other TNF-α inhibitors are anti-TNF monoclonal antibodies and include infliximab, adalimumab, golimumab, and certolizumab pegol. Most clinical trials have used etanercept in patients who have failed traditional DMARDs. Immunizations must be current prior to administration; TB skin tests (PPD) should be performed prior to and during therapy, and latent TB should be treated prior to administering etanercept; avoid live vaccines concurrently. Subcutaneous dosing: 50 mg once weekly; or 25 mg given twice weekly (individual doses should be separated by 72-96 hours).

A 54-year-old woman presents to the pharmacy seeking a recommendation for the osteoarthritis (OA) in her knee. She says that the condition was recently diagnosed at her doctor's office. Before using oral medications, the PCP told the patient to try a set of exercises and walking to stretch and strengthen muscles around the joint. The patient reports that she has started these activities, but needs something to help with her mild to moderate pain in the meantime. Her past medical history includes hypertension and dyslipidemia.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; lisinopril 10 mg tablet 1 po daily; simvastatin 10 mg tablet 1 po daily at night

Physical Exam/Other Studies:

None available

Physical exam reveals an overweight woman in no acute distress.

The patient does not want to start an oral medication at this time, but is interested in an OTC topical agent to help with her pain. You tell the patient to follow up with her PCP for further pain assessment, but recommend a product that may help.

What is an appropriate OTC topical agent to most effectively treat her pain?

Capsaicin	Topical analgesic
Mechanism of Action	Induces release of substance P from peripheral sensory neurons; after repeated application, capsaicin depletes the neuron of substance P and prevents re-accumulation; this leads to less transmission of pain impulses from the periphery to the CNS by substance P.
***Contraindications*/ Precautions**	*Hypersensitivity*/For external use only; avoid contact with eyes or mucous membranes; should not be applied to broken or irritated skin; treated area should not be exposed to heat or direct sunlight; affected area should not be bandaged; transient burning may occur and generally disappears after several days; discontinue use if severe burning develops
Adverse Effects	Erythema, pain, transient hypertension, pruritus, nausea, vomiting
Drug Interactions	None known
Monitoring	For efficacy and adverse effects
Case Notes	While lifestyle modifications can be effective, especially in early and mild OA, patients sometimes need analgesics to help with pain that exists prior to the expected benefits from exercise. Topical capsaicin has been shown to be effective for pain relief versus placebo in controlled studies. Other topicals containing methylsalicylate may have modest and short-term efficacy for acute OA pain. Dosing for cream, gel, liquid, or lotion: Apply to affected area three to four times/day; efficacy may be decreased if used less than three times/day; best results seen after two to four weeks of continuous use. The topical patch is used for other indications and carries cardiovascular and cerebrovascular precautions. Counsel patients to wear gloves during application and to wash hands with soap and water after applying to avoid spreading to eyes or other sensitive areas of the body.

A 48-year-old woman presents to the pharmacy seeking assistance with osteoarthritis (OA) pain in her knee. She does not visit the doctor often and has no significant past medical history. Her OA was diagnosed a few months ago, and she has been doing prescribed exercises to help maintain range of motion and improve strength and stretch of local muscles. She has been using acetaminophen only occasionally as she does not like to use manufactured medications and believes strongly in the principles of natural medicine. When her PCP offered her an NSAID for pain, she opted to try exercises.

Allergies: NKDA

Medications: Acetaminophen 500 mg tablet (OTC) 1 po every four to six hours as needed (not to exceed 4,000 mg per day)

Physical Exam/Other Studies:

None available

Physical exam reveals an overweight woman in no acute distress.

The patient is not interested in an OTC "medication," and wants you to recommend an OTC herbal or natural product that could help with her OA.

What is the most appropriate natural OTC product that you could recommend that may provide some benefit?

Glucosamine	Nutraceutical; an amino-sugar
Mechanism of Action	Glucosamine is involved in the synthesis of glycolipids, glycoproteins, hyaluronic acid, proteoglycans, and glycosaminoglycans, which are the major structural components of cartilage. Naturally produced in humans, it is important for maintaining elasticity, strength, and resiliency of the cartilage in articular joints.
***Contraindications/* Precautions**	*Hypersensitivity to shellfish, active bleeding*/History of bleeding, hemostatic disorders, renal impairment or diabetes; use with anticoagulants, antiplatelet drugs, aspirin, or NSAIDs
Adverse Effects	Drowsiness, insomnia, somnolence, GI discomfort, possibly glucose elevation
Drug Interactions	Hypoglycemic agents, antineoplastic agents, diuretics, CNS depressants, anticoagulants, antiplatelet drugs, aspirin, and NSAIDs
Monitoring	Efficacy and adverse effects
Case Notes	While lifestyle modifications can be effective, especially in early and mild OA, often patients will seek additional treatments for relief of pain. Glucosamine has long been used and studied for effectiveness in OA. Study results are conflicting regarding the effectiveness of glucosamine; however, the safety profile of this medication makes it an appealing option and worth consideration when options are limited. Glucosamine may work synergistically with another natural product chondroitin. Dosing: 500 mg three to four times a day; should be at least 1,500 mg a day of glucosamine with or without 1,200 mg a day of chondroitin. Discontinue use prior to dental or surgical procedures due to bleeding risk (generally at least 14 days before). Glucosamine may be obtained from shellfish so those with shellfish allergy should avoid use. Since these natural products are not FDA regulated, efficacy and safety could be compromised by varying doses from products.

A 56-year-old woman presents to her PCP's office to discuss treatment options of the osteoarthritis (OA) in her hands. Acetaminophen was used initially in her treatment, but eventually became ineffective at controlling her pain. For the past year, ibuprofen has successfully controlled her pain and allowed her to use her hands with minimal limitations. However, two weeks ago, she stopped her ibuprofen because it was irritating her stomach. She currently rates her pain at 4 on a scale of 10 and has morning stiffness for about 20 minutes each day. Her past medical history includes OA and low back pain.

Allergies: NKDA

Medications: Ibuprofen 800 mg tablet 1 po three times daily (currently on hold); calcium carbonate 600 mg tablet (OTC) 1 po twice daily; vitamin D 400 units (OTC) po twice daily

Physical Exam/Other Studies:

Wt 128 lb Ht 67 in T 98.6°F BP 114/70 HR 68 RR 12 O_2 sat 99%

Physical exam reveals a thin woman in no acute distress; Heberden nodes noted at several distal interphalangeal joints of each hand.

She was happy with the success of ibuprofen, but feels she just cannot take it anymore due to stomach upset. She would like a new oral medication and is hoping to keep her number of prescriptions to a minimum as she "doesn't like to take too many medications."

Which of the following is the most appropriate therapeutic option at this time?

A. continue ibuprofen and add omeprazole
B. continue ibuprofen and add misoprostol
C. stop ibuprofen and switch to celecoxib
D. stop ibuprofen and switch to oxycodone

Celecoxib	COX-2 inhibitor (cyclooxygenase-2 selective inhibitor)
Mechanism of Action	Inhibits prostaglandin synthesis by decreasing the activity of the COX-2 enzyme without inhibiting the COX-1 enzyme; allows antipyretic, analgesic, and anti-inflammatory properties
***Contraindications/* Precautions**	*Hypersensitivity to celecoxib, sulfonamides, aspirin, other NSAIDs; perioperative pain for coronary artery bypass graft (CABG) surgery/*Hepatic or renal impairment, aspirin-sensitive asthma; NSAIDs are associated with an increased risk of adverse cardiovascular thrombotic events, including MI and stroke; avoid use in heart failure; NSAIDs may increase risk of gastrointestinal irritation, ulceration, bleeding, and perforation; anemia, skin reactions, HTN
Adverse Effects	Hypertension, headache, diarrhea, edema, fever, skin rash, nausea, gastroesophageal reflux, abdominal pain, arthralgia
Drug Interactions	Substrate of CYP2C9 and 3A4; inhibits CYP2C8 and 2D6; see product labeling for multiple interactions
Monitoring	CBC, hepatic function with LFT, renal function with blood chemistry
Case Notes	In patients with OA who have failed acetaminophen and are at higher risk of GI complications from NSAID use, any of options A, B, or C are appropriate. Based on this patient's requests or needs, switching to one singe agent (celecoxib) instead of adding a new medication with ibuprofen is more desirable. When using COX-2 inhibitors, both GI and cardiovascular risks must be considered. A former COX-2 inhibitor, rofecoxib, was removed from the market in 2004 due to increased cardiovascular risks; however, it may have provided a reduced GI risk compared to nonspecific NSAIDs. This patient has no cardiovascular disease in her history and needs a treatment that may be of less GI risk. This makes celecoxib an option at this time. Oral dose for OA: 200 mg/day as a single dose or in two divided doses. Other indications may use different doses. Reduce dose 50% in moderate hepatic impairment. Do not use in severe hepatic or renal impairment.

A 55-year-old woman presents to her PCP complaining of increased osteoarthritis (OA) pain in her knee. Her past medical history is significant for Type 2 diabetes, hypertension, dyslipidemia, and OA. She tried acetaminophen as a first-line agent, but had no success. Prescription strength NSAIDs had been effective, but for the past three months, she cannot get relief. She has been exercising regularly and even working with a physical therapist for her knee. She is hoping to avoid having to use opioid analgesics, but is in need of pain relief.

Allergies: NKDA

Medications: Metformin 1,000 mg tablet 1 po twice daily; insulin glargine inject 32 units subcutaneously every night; enalapril 10 mg tablet 1 po twice daily; hydrochlorothiazide 25 mg tablet 1 po daily; amlodipine 5 mg tablet 1 po daily; lovastatin 40 mg tablet 1 po every night; ibuprofen 800 mg tablet 1 po three times daily

Physical Exam/Other Studies:

Wt 180 lb Ht 66 in T 98.6°F BP 128/78 HR 76 RR 12 O_2 sat 99%

Physical exam reveals an overweight woman in no acute distress.

A1c 8.6% LDL 94 TG 148 HDL 42 K 4.1 SCr 0.9

X-ray shows joint space narrowing and marginal osteophytes.

The patient is willing to receive intra-articular injections to attempt to gain improvement. The PCP would like to avoid using corticosteroid injections, which would likely worsen her already uncontrolled diabetes.

What other product could be used for intra-articular injection as a step before resorting to opioid analgesics?

Hyaluronic Acid (hyaluronate)	Antirheumatic (natural polysaccharide)
Mechanism of Action	A polysaccharide that is distributed widely in the extracellular matrix of connective tissues; acts as a tissue and/or joint lubricant to temporarily increase viscosity; since hyaluronic acid concentration is decreased in OA joints, it is thought that injections may reconstitute synovial fluid and reduce symptoms of OA.
***Contraindications*/ Precautions**	*Hypersensitivity to hyaluronic acid or to avian proteins (egg products, feathers), knee joint infections, skin infection at injection site*/Remove effusion, if present, prior to injection; do not inject extra-articularly or into synovium; use with caution if venous or lymphatic stasis is present in the leg; do not use disinfectants containing quaternary salts for skin preparation as this may cause precipitation of hyaluronic acid.
Adverse Effects	Arthralgia, joint effusion, back pain, tendonitis, paresthesia, nausea, fatigue, increased blood pressure
Drug Interactions	None known
Monitoring	Adverse effects and efficacy
Case Notes	Intra-articular hyaluronic acid injections for OA of the knee may provide a decrease in pain. While some study results are conflicting, injections have demonstrated efficacy for more than six months following an injection series. Injections with hyaluronic acid may be beneficial for patients with knee OA unresponsive to other therapies. Products are injected weekly from one to five weeks depending on the product. Not for IV use. Other formulations are available for other indications and may carry other contraindications, precautions, or adverse effects.

A 54-year-old man presents to his PCP's office one morning having an acute gout attack. His past medical history includes hypertension. He awoke at 4 AM in excruciating pain. His left great toe was red, swollen, and warm to the touch; he could not stand to even let the bed sheets touch his foot. He would have gone to the emergency room, but did not have means of transportation; a friend brought him to the office this morning. He reports having one previous episode two years ago that presented just like this.

Allergies: Aspirin and other NSAIDs (rash and swelling)

Medications: Lisinopril 40 mg tablet 1 po daily; amlodipine 10 mg tablet 1 po daily; hydrochlorothiazide 25 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 215 lb Ht 70 in T 99.8°F BP 152/94 HR 102 RR 18 O_2 sat 99%

Physical exam reveals an overweight man in great pain. His left great toe (metatarsophalangeal joint) is swollen, warm, erythematous, and very sensitive to touch or motion.

Synovial fluid is positive for monosodium urate crystals.

What medication do you recommend for treatment of his acute gout exacerbation?

Colchicine	Antigout agent
Mechanism of Action	Inhibits neutrophil function and inflammatory response to urate crystals
***Contraindications/* Precautions**	*Hypersensitivity; concomitant use of a P-glycoprotein (P-gp) or strong CYP3A4 inhibitor in presence of renal or hepatic impairment/*Hepatic impairment, renal impairment, blood dyscrasias, neuromuscular toxicity, GI symptoms
Adverse Effects	Diarrhea, abdominal pain, cramping, nausea, vomiting, myopathy, neuropathy, renal failure, hepatic failure, bone marrow suppression, thrombocytopenia (rare)
Drug Interactions	Substrate of CYP3A4 and P-glycoprotein; induces CYP2C8, 2C9, 2E1, 3A4; avoid grapefruit juice; adjust colchicine dose if taking macrolide, azole antifungals, select statins, verapamil, diltiazem, protease inhibitors, cyclosporine; see product labeling for multiple interactions
Monitoring	CBC, hepatic function, renal function
Case Notes	While NSAIDs are effective and typically better tolerated, colchicine can be used as a first-line agent for a gout exacerbation. In this case, the NSAID must be avoided due to allergy. Oral corticosteroids may be used, but only if other drugs are contraindicated or ineffective. Diuretics may increase uric acid levels, so consider replacing his hydrochlorothiazide with another antihypertensive agent. Dosing for initial flare treatment: 1.2 mg at the first sign of flare, followed in one hour with a single dose of 0.6 mg. Colchicine is sometimes used for chronic prophylaxis; the prophylaxis dose is: 0.6 mg once or twice daily. See product labeling for dosage adjustment for concomitant therapy with CYP3A4 or P-glycoprotein (P-gp) inhibitors. GI adverse effects often limit use.

A 44-year-old man presents to his PCP's office one month following an acute gout exacerbation that was treated at the emergency department. His past medical history includes hypertension and dyslipidemia. This was his third gout attack this year. He is currently in no pain, but wants to take preventative action as these attacks impact his life greatly. The hospital treated his acute gout flare with indomethacin, which he took for about 10 days. He has used colchicine in the past but does not tolerate it due to significant diarrhea.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; niacin 500 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 180 lb Ht 70 in T 98.6°F BP 120/72 HR 78 RR 12 O_2 sat 99%

Physical exam reveals a male in no acute distress.

The patient wants to be put on a medication to help prevent gout flares. He refuses chronic NSAID use due to his hypertension and worries about losing his kidney function, which is currently fine.

What medication do you recommend for prevention of acute gout exacerbations?

Allopurinol	Xanthine oxidase inhibitor (allopurinol and febuxostat)
Mechanism of Action	Inhibits xanthine oxidase to reduce production of uric acid
***Contraindications*/ Precautions**	*Hypersensitivity; for febuxostat, use with azathioprine, mercaptopurine, or theophylline/*Rash, bone marrow suppression, hepatotoxicity, renal impairment, risk of hypersensitivity increased by use of ACE inhibitors, diuretics, amoxicillin/ampicillin; dose adjust allopurinol if taking mercaptopurine or azathioprine; watch for thromboembolic events with febuxostat
Adverse Effects	Rash, acute gout, diarrhea, nausea; more rarely: leukopenia, renal or hepatic toxicity; for febuxostat, liver function abnormalities, arthralgias
Drug Interactions	Avoid didanosine; may decrease metabolism of mercaptopurine and azathioprine; ACE inhibitors, diuretics, amoxicillin, ampicillin, cyclophosphamide, antacids, theophylline, warfarin, carbamazepine, anticonvulsants; avoid didanosine, mercaptopurine, azathioprine, or theophylline with febuxostat
Monitoring	CBC, hepatic and renal function, serum uric acid levels; LFT at two and four months (febuxostat)
Case Notes	Allopurinol is commonly used as prophylaxis for gout flares. Low doses of colchicine, NSAIDs, or oral corticosteroids may also be used. Diuretics and niacin may increase uric acid levels, so consider replacing his hydrochlorothiazide with another antihypertensive agent and his niacin with another lipid-lowering agent. Allopurinol oral dose: Mild: 200-300 mg/day; Severe: 400-600 mg/day; initiate dose at 100 mg/day and increase weekly to recommended dosage. Maximum daily dose: 800 mg/day. Febuxostat oral dose: 40 mg once daily; may increase to 80 mg once daily in patients who do not achieve a serum uric acid level <6 mg/dL after two weeks. See product labeling for specific dosing adjustments for renal impairment. Allopurinol is not effective when used intermittently and should be used for long-term prophylaxis.

A 34-year-old woman presents to her PCP's office for a routine follow-up of her systemic lupus erythematosus (SLE). Her past medical history is significant only for SLE. Her SLE has been fairly mild and well managed with routine NSAID use, but more recently, this has not been adequate to control her symptoms. She complains of more frequent fatigue and muscle and joint pains, and her skin has been more sensitive to the sunlight, leaving a scaly red skin rash. She has a butterfly-shaped rash across the bridge of her nose. She is hoping for a new treatment option today.

Allergies: NKDA

Medications: Ibuprofen 800 mg tablet 1 po three times daily

Physical Exam/Other Studies:

Wt 134 lb Ht 66 in T 100.0°F BP 122/84 HR 88 RR 14 O_2 sat 99%

Physical exam reveals a thin woman with cutaneous manifestations of SLE including a malar rash.

Eye exam is normal.

Since there is currently no sign of organ damage, there is not yet any need to consider treatment with a cytotoxic agent.

What medication do you recommend for treatment of her mild to moderate SLE?

Hydroxychloroquine	Aminoquinoline and antimalarial (hydroxychloroquine, chloroquine)
Mechanism of Action	Mechanism in SLE is uncertain; may interfere with T-lymphocyte activation, inhibit cytokines, decrease sensitivity to ultraviolet light, anti-inflammatory activity
***Contraindications*/ Precautions**	*Hypersensitivity; retinal or visual field changes attributable to 4-aminoquinolines; long-term use in children*/Hepatic impairment, alcoholism, or concurrent therapy with hepatotoxic agents; porphyria; psoriasis; G6PD deficiency; may cause ophthalmic, cardiac, hematologic, or neurologic effects; should be prescribed by physicians familiar with its use
Adverse Effects	Cardiomyopathy (rare), dizziness, nightmares, nervousness, rash, alopecia, abdominal cramping, diarrhea, nausea, vomiting, weight loss, agranulocytosis, aplastic anemia, hemolysis, leukopenia, thrombocytopenia, hepatic impairment, myopathy, weakness, retinopathy and other optical disturbances, tinnitus, deafness, bronchospasm
Drug Interactions	Avoid use with other antimalarials, immunosuppressants, or live vaccines; see product labeling for numerous interactions
Monitoring	CBC, hepatic function, muscle strength, ophthalmologic exam
Case Notes	The typical treatment for mild to moderate SLE is an NSAID, hydroxychloroquine, or low-dose oral corticosteroid. Arthralgias and cutaneous manifestations are generally well managed with hydroxychloroquine. However, it may take three to six months to take full effect. It may be necessary to increase the NSAID dose, try another NSAID, or add a low dose of oral corticosteroid to "bridge" until the hydroxychloroquine has taken effect. Dose for SLE is 200-400 mg daily (doses vary for other indications). Gradual tapering of the dose may be attempted generally after one to two years of treatment. Due to the potential retinal toxicity, an ophthalmologic exam should be done every 3-12 months.

A 36-year-old woman presents to her PCP's office to discuss her systemic lupus erythematosus (SLE) with renal complications (lupus nephritis). She was diagnosed with SLE five years ago and has had mild lupus nephritis (WHO classification II) for the past year treated with corticosteroids. Her past medical history is significant for SLE with nephritis and hypertension. She is complaining of increased fatigue, fevers, and joint pains. She has a red skin rash on her arms and face, and her lower legs are swollen.

Allergies: NKDA

Medications: Prednisone 20 mg tablet 2 po daily; lisinopril 20 mg tablet 1 po daily

Physical Exam/Other Studies:

Wt 165 lb Ht 67 in T 100.2°F BP 152/94 HR 86 RR 14 O_2 sat 99%

Physical exam reveals a thin woman with cutaneous manifestations of SLE, worsened arthritic pain, and 2+ pitting edema bilaterally.

SCr 2.2 microalbumin:creatinine 1,250 mg/g

With her worsened SLE symptoms in addition to lower extremity edema, proteinuria, and elevated blood pressure and serum creatinine, her lupus nephritis is re-classified. She is now classified with diffuse proliferative nephritis (WHO classification IV), which is more advanced and has a higher risk for loss of renal function.

What is the standard treatment, in combination with corticosteroids, for this class of lupus nephritis?

Cyclophosphamide	Antineoplastic, alkylating agent, nitrogen mustard, immunosuppressant (cyclophosphamide, ifosfamide)
Mechanism of Action	Alkylation and cross-linking DNA strands, inhibiting DNA replication
***Contraindications*/ Precautions**	*Hypersensitivity*/Bone marrow suppression, impaired renal or hepatic function
Adverse Effects	Alopecia, hyponatremia, nausea, vomiting, mucositis, hemorrhagic cystitis, nephrotoxicity, hepatotoxicity, sterility, secondary tumors
Drug Interactions	CYP2B6 and 3A4 substrate, CYP3A4 inhibitor
Monitoring	CBC, urinalysis, serum electrolytes, serum creatinine, urine specific gravity, urine output
Case Notes	Cyclophosphamide combined with prednisone has become standard treatment for WHO class III and IV lupus nephritis. Cyclophosphamide improves long-term outcomes of lupus nephritis (decreased risk of end-stage renal disease or dialysis) and also helps stabilize extrarenal symptoms. Other drugs sometimes used include azathioprine and mycophenolate mofetil. Dosing for lupus nephritis: 1-3 mg/kg oral therapy or 0.5-1 g/m^2 IV therapy; IV therapy is common but not proven more effective than oral. It is dosed monthly for six months, then every three months for one to two years once in remission (based on expert opinion). Mesna routinely is given with cyclophosphamide doses greater than 1 g/m^2 and any dose of ifosfamide to prevent hemorrhagic cystitis. Cyclophosphamide and all alkylating agents are known to cause decreased or absent fertility and have been associated with secondary cancers. Cyclophosphamide's emetogenic potential depends on the dose, with doses <750 mg/m^2 considered moderate, doses of 750-1,500 mg/m^2 considered moderately high, and doses ≥1,500 mg/m^2 considered highly emetogenic. This can be managed with oral ondansetron plus dexamethasone.

A 65-year-old woman returns to her PCP's office to discuss the results of her central DXA scan and a new diagnosis of osteoporosis. The DXA scan was done due to her age, but other risk factors include gender, cigarette smoking, low body weight, and a sister who suffered a hip fracture. Her past medical history is significant for hypertension, dyslipidemia, a myocardial infarction eight years ago, and osteoarthritis.

Allergies: NKDA

Medications: Metoprolol tartrate 100 mg tablet 1 po twice daily; lisinopril 40 mg tablet 1 po daily; atorvastatin 40 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; acetaminophen 325 mg tablet 1 po four times daily

Physical Exam/Other Studies:

Wt 112 lb Ht 64 in T 98.6°F BP 114/72 HR 64 RR 14 O_2 sat 98%

Central DXA scan T-score (hip): –2.7

Physical exam reveals a thin elderly woman in no acute distress.

She is counseled to reduce cola and other carbonated beverage intake, limit alcohol intake to no more than one drink a day, increase fruit and vegetable intake, stop smoking, and participate in weight-bearing exercise daily. She is started on calcium carbonate for 1,200 mg of elemental calcium per day as well as vitamin D 1,000 units per day.

What class of prescription medication is considered first line in prevention of osteoporotic bone fractures and should be added at this time?

Bisphosphonates	Alendronate, ibandronate, risedronate, zoledronic acid (IV)
Mechanism of Action	Decreases the rate of bone resorption, leading to an increase in bone mineral density
***Contraindications*/ Precautions**	*Hypersensitivity, hypocalcemia, inability to stay in an upright position for 30 minutes (60 minutes for ibandronate), esophageal strictures or achalasia, Clcr <35mL/min*/Renal impairment, ensure adequate calcium intake and normocalcemia, severe bone or muscle pain
Adverse Effects	Hypocalcemia, hypophosphatemia, headache, acid reflux, GERD, esophageal or gastric ulcer, dyspepsia, nausea, diarrhea, constipation, musculoskeletal pain, may irritate upper GI mucosa; rare: osteonecrosis of the jaw
Drug Interactions	NSAIDs, aspirin, antacids containing calcium, aluminum, and magnesium; aminoglycosides, phosphate supplements, calcium salts
Monitoring	Bone mineral density, height, weight, fractures, adverse effects
Case Notes	Bisphosphonates are considered first line in prevention of osteoporotic bone fractures and have provided the greatest fracture risk reductions and bone mineral density increases. Second- and third-line agents include raloxifene, teriparatide, or calcitonin. Oral agents must be taken 30 minutes (60 minutes for ibandronate) prior to the morning meal and medications/supplements and with at least 6 ounces of plain water. The patient must remain in an upright position during that time frame to reduce risk of esophageal damage. Different bisphosphonate formulations allow for daily, weekly, monthly, or quarterly dosing. Alendronate oral dosing: Prophylaxis: 5 mg once daily or 35 mg once weekly; Treatment: 10 mg once daily or 70 mg once weekly. Risedronate oral dosing for prevention or treatment: 5 mg once daily, 35 mg once weekly, or 150 mg once a month. Ibandronate dosing for prevention or treatment: Oral: 2.5 mg once daily or 150 mg once a month; IV: 3 mg every three months. Dosing varies for males and other indications. Other bisphosphonates exist for other indications.

A 68-year-old woman presents to her PCP's office to determine a drug therapy for her newly diagnosed osteoporosis. A central DXA scan was done due to her age and risk factors including gender, low body weight, and a sister with a vertebral fracture. Her past medical history is significant for low back pain, hypertension, dyslipidemia, Type 2 diabetes, and GERD. She has never smoked cigarettes.

Allergies: NKDA

Medications: Hydrochlorothiazide 25 mg tablet 1 po daily; lisinopril 30 mg tablet 1 po daily; pravastatin 40 mg tablet 1 po daily at bedtime; aspirin 81 mg tablet (OTC) 1 po daily; ibuprofen 800 mg tablet 1 po three times daily as needed; cyclobenzaprine 5 mg tablet 1 po three times daily as needed; omeprazole 20 mg tablet (OTC) 1 po daily; metformin 500 mg tablet 1 po twice daily; glipizide 2.5 mg tablet 1 po twice daily

Physical Exam/Other Studies:

Wt 120 lb Ht 65 in T 98.5°F BP 122/78 HR 74 RR 12 O_2 sat 99%

Central DXA scan T-score (hip): –2.6

Physical exam reveals a thin elderly woman in no acute distress.

She is counseled to reduce cola and other carbonated beverage intake, limit alcohol intake to no more than one drink a day, increase fruit and vegetable intake, and participate in weight-bearing exercise daily. She is started on calcium carbonate for 1,200 mg of elemental calcium per day as well as vitamin D 1,000 units per day.

She wants an oral medication and does not believe she can remain in an upright position for very long in the mornings due to her back pain.

What oral prescription medication is most appropriate to start for prevention of osteoporotic fractures?

Raloxifene	Mixed estrogen agonist/antagonist
Mechanism of Action	Estrogen agonist on bone and antagonist on breast and uterine tissue; decreases bone resorption, increasing bone mineral density and decreasing fracture incidence
***Contraindications*/ Precautions**	*Hypersensitivity, a venous thromboembolic (VTE) disorder, pregnancy, women of child-bearing potential (premenopausal), breastfeeding*/Cardiovascular disease increases risk of stroke, history of hypertriglyceridemia, use with estrogen, high risk of VTE, prolonged immobilization
Adverse Effects	Peripheral edema, hot flashes, arthralgias, flu-like syndrome, chest pain, VTE, insomnia, breast pain, rash, weight gain, abdominal pain, vomiting, vaginal bleeding, urinary tract disorder, bronchitis, sinusitis, diaphoresis, tendon disorder, pharyngitis, pneumonia
Drug Interactions	Bile acid sequestrants and levothyroxine
Monitoring	Bone mineral density; lipid profile; if abnormal vaginal bleeding, perform diagnostic measures
Case Notes	Bisphosphonates are considered first line in prevention of osteoporotic bone fractures and have provided the greatest fracture risk reductions and bone mineral density increases. Second- and third-line agents include raloxifene, teriparatide, and calcitonin. The patient prefers an oral agent, but cannot remain upright for at least 30 minutes. This excludes bisphosphonates as a treatment option. The most appropriate second-line agent is raloxifene. However, if a fracture is already present or if a very low T-score (<–3.5) is found, teriparatide may be used as a first-line therapy. Raloxifene is only indicated for use in women and should be dosed 60 mg once daily This drug class used to be referred to as selective estrogen receptor modulators or SERMs. There are other related agents in this grouping (clomiphene, tamoxifen, and toremifene) used for other indications, such as high risk of invasive breast carcinoma or treatment of metastatic breast cancer.

A 70-year-old woman presents to her PCP's office a week after a visit to the emergency room for a low-trauma wrist fracture. A central DXA scan was done revealing a very low T-score. She has been taking calcium and vitamin D for several years. She quit smoking 20 years ago. Her past medical history is significant for hypertension, Type 2 diabetes, and osteoarthritis.

Allergies: NKDA

Medications: Hydrochlorothiazide 12.5 mg tablet 1 po daily; lisinopril 40 mg tablet 1 po daily; aspirin 81 mg tablet (OTC) 1 po daily; ibuprofen 800 mg tablet 1 po three times daily as needed; metformin 1,000 mg tablet 1 po twice daily; glipizide 10 mg tablet 1 po twice daily; calcium carbonate 600 mg tablet 1 po twice daily; vitamin D 400 units po twice daily

Physical Exam/Other Studies:

Wt 110 lb Ht 64 in T 98.6°F BP 128/78 HR 78 RR 12 O_2 sat 99%

Central DXA scan T-score (hip): –3.6

Physical exam reveals a thin elderly woman in no acute distress.

She is counseled to reduce cola and other carbonated beverage intake, limit alcohol intake to no more than one drink a day, increase fruit and vegetable intake, and participate in weight-bearing exercise daily.

She is very concerned about her future fracture risk and is willing to do whatever is necessary for prevention.

Other than a bisphosphonate, what prescription medication is appropriate to start first line for treatment and prevention of osteoporotic fractures in this patient?

Teriparatide	Parathyroid hormone (PTH) analogue
Mechanism of Action	Similar to the physiologic activity of PTH; increases bone formation, bone remodeling rate, osteoblast number and activity, and bone mass (only medication to increase bone formation)
***Contraindications*/ Precautions**	*Hypersensitivity; avoid use in patients with an increased risk of osteosarcoma (including Paget's disease, prior radiation, unexplained elevation of alkaline phosphatase, or in patients with open epiphyses); history of skeletal metastases, hyperparathyroidism, or pre-existing hypercalcemia*/Risk of orthostatic hypotension, active or recent urolithiasis
Adverse Effects	Hypercalcemia, orthostatic hypotension, syncope, chest pain, dizziness, nausea, hyperuricemia, vomiting, arthralgia, weakness, rhinitis, pharyngitis, dyspepsia, pneumonia, rash, insomnia, depression
Drug Interactions	None known
Monitoring	Serum calcium, serum phosphorus, uric acid, blood pressure, bone mineral density
Case Notes	Bisphosphonates are considered first line in prevention of osteoporotic bone fractures and provide the greatest fracture risk reductions and bone mineral density increases. Second- and third-line agents include raloxifene, teriparatide, and calcitonin. However, for treatment of a low-trauma fracture and prevention of fractures in patients with T-scores <–3.5, teriparatide may be used first line instead of bisphosphonates. Available in an injection pen device; dose: inject 20 mcg subcutaneously once daily in the thigh or abdomen; rotate injection sites. First dose should be given sitting or lying down in case of orthostatic hypotension. It should be stored in the refrigerator. Discard after 28 days of use. Teriparatide is expensive compared to other treatment options. See black box warning for osteocarcinoma in animals. Use beyond two years has not been studied and is not recommended.

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